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T06217-0903550

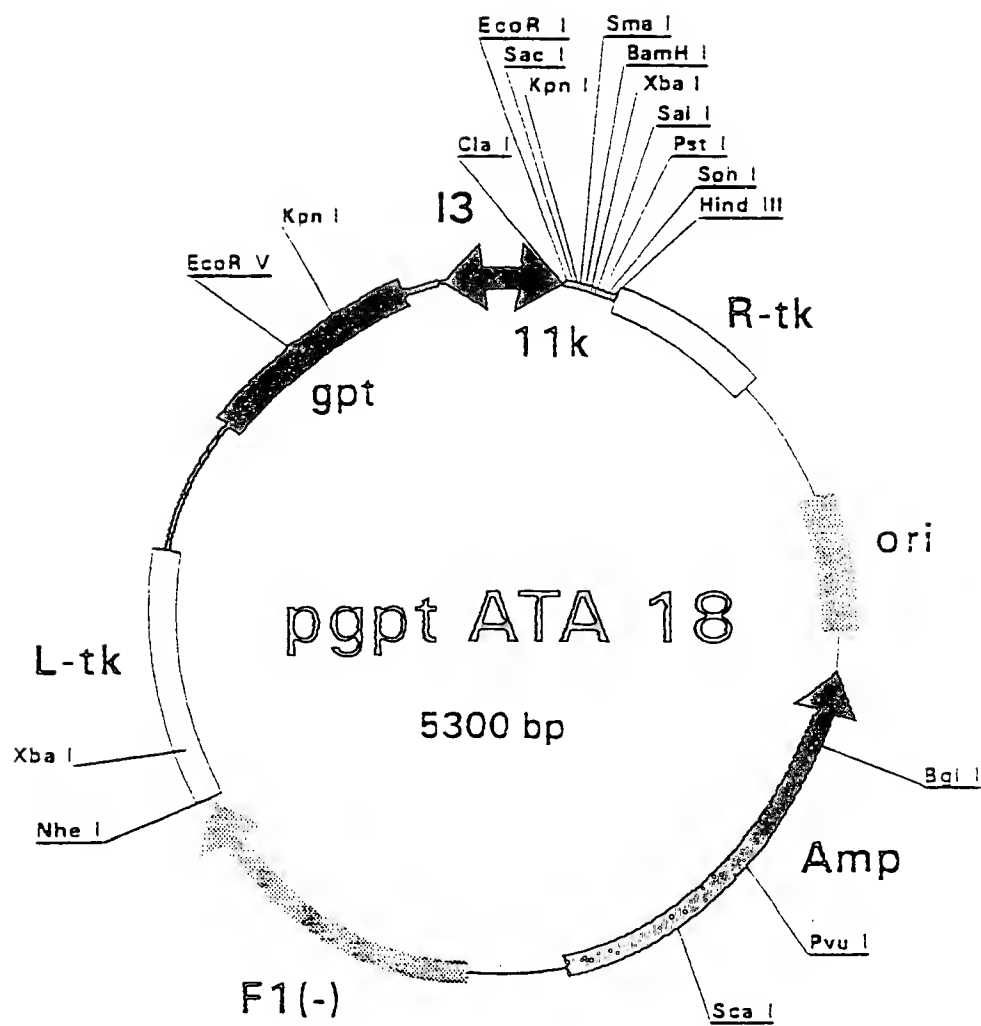


Fig. 1

FOUO "00055550

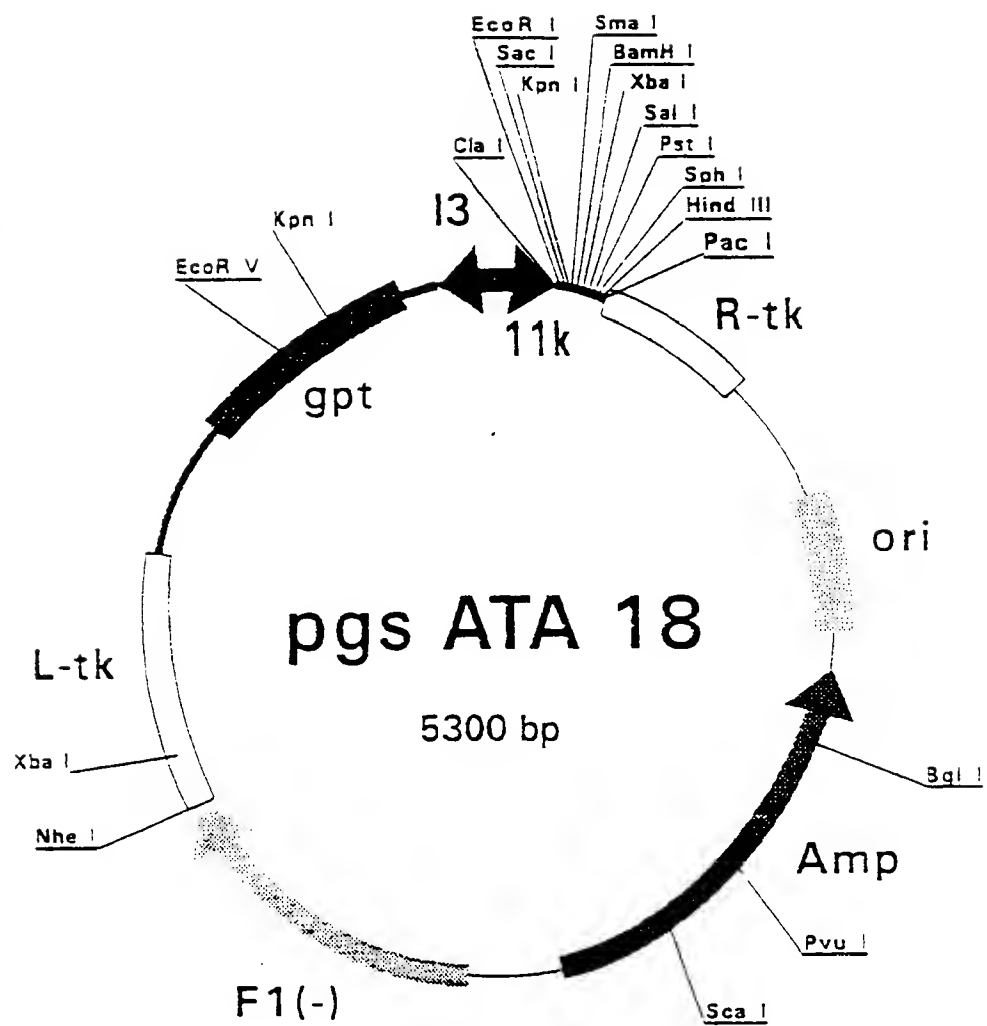


Fig. 2

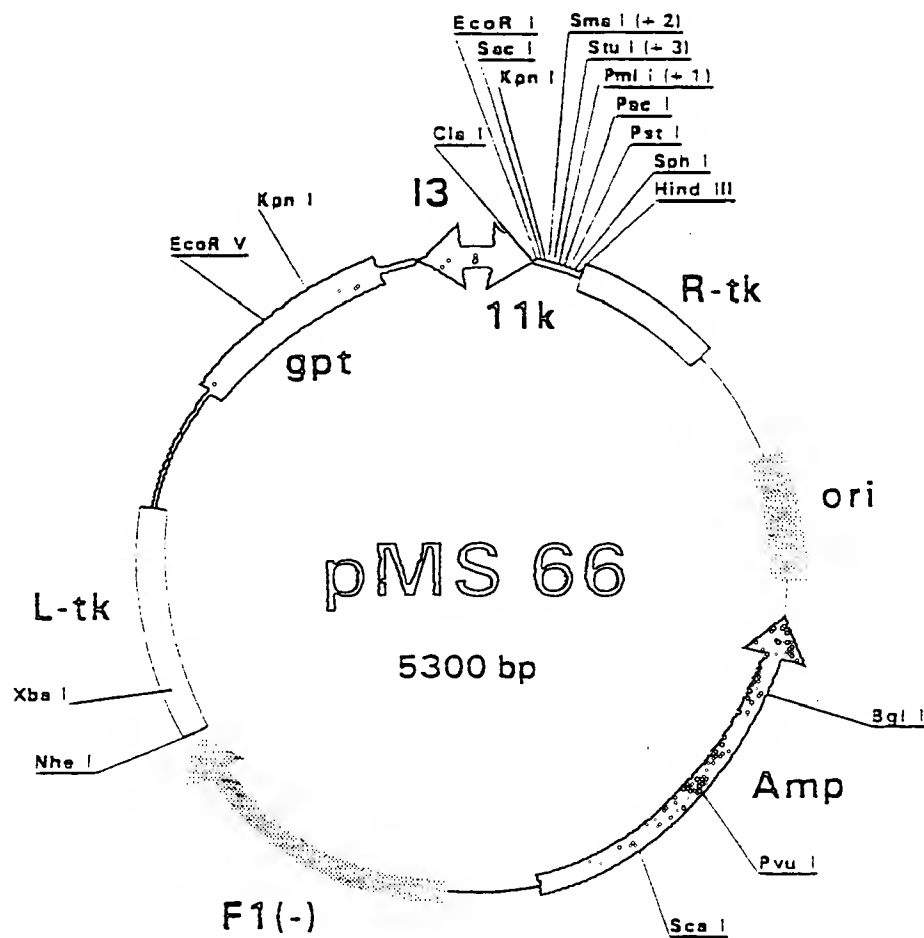


Fig. 3

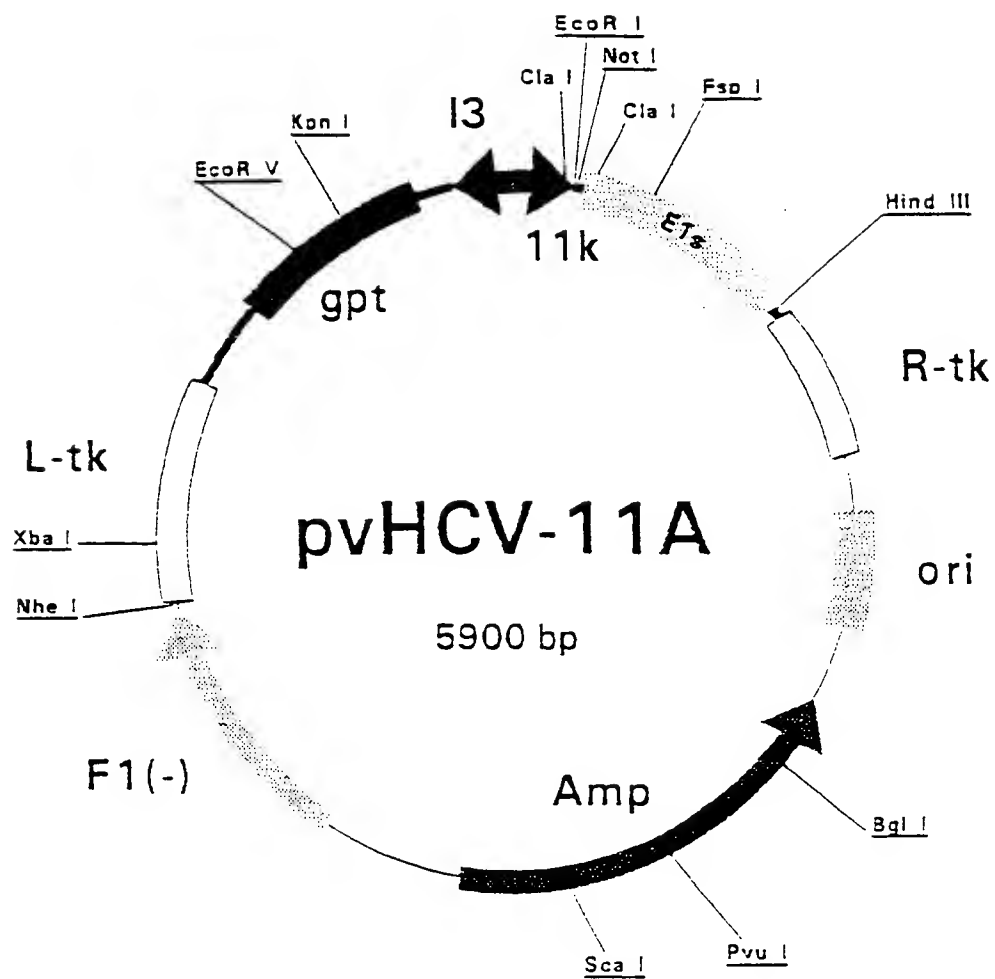


Fig. 4

Anti-E1 levels in NON-responders to IFN treatment

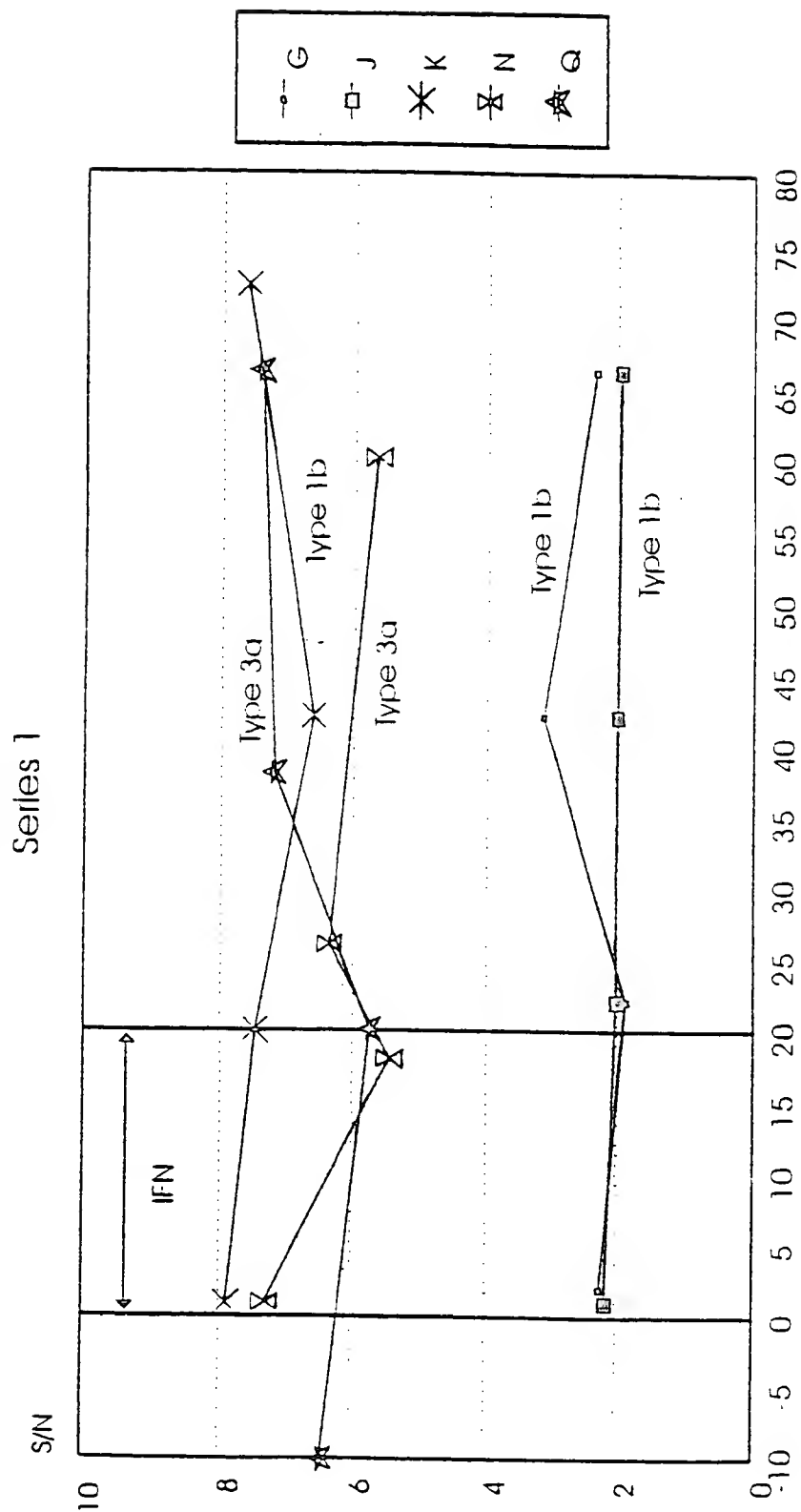
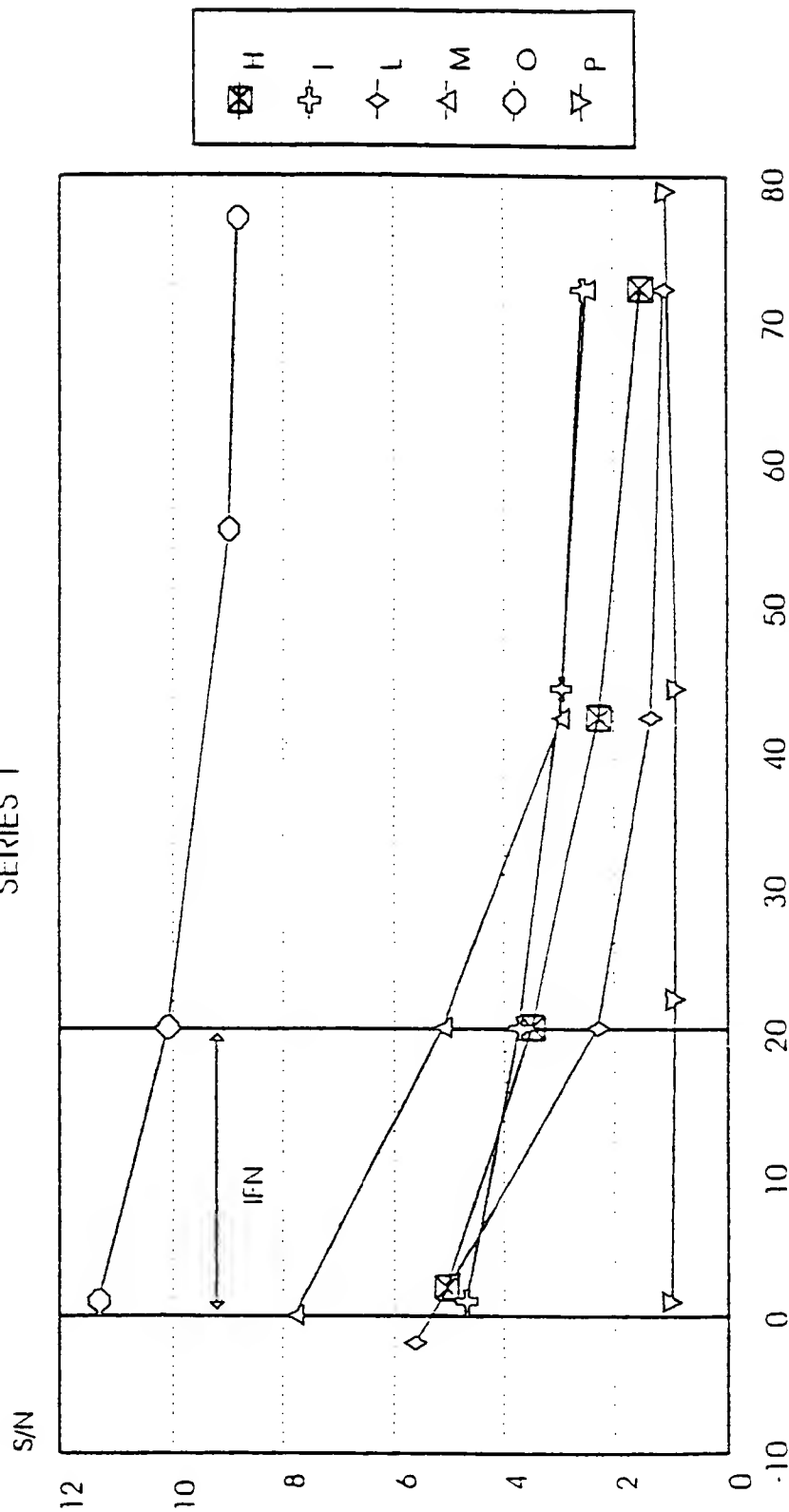


Fig. 5

Anti-E1 levels in RESPONDERS to IFN treatment

SERIES 1

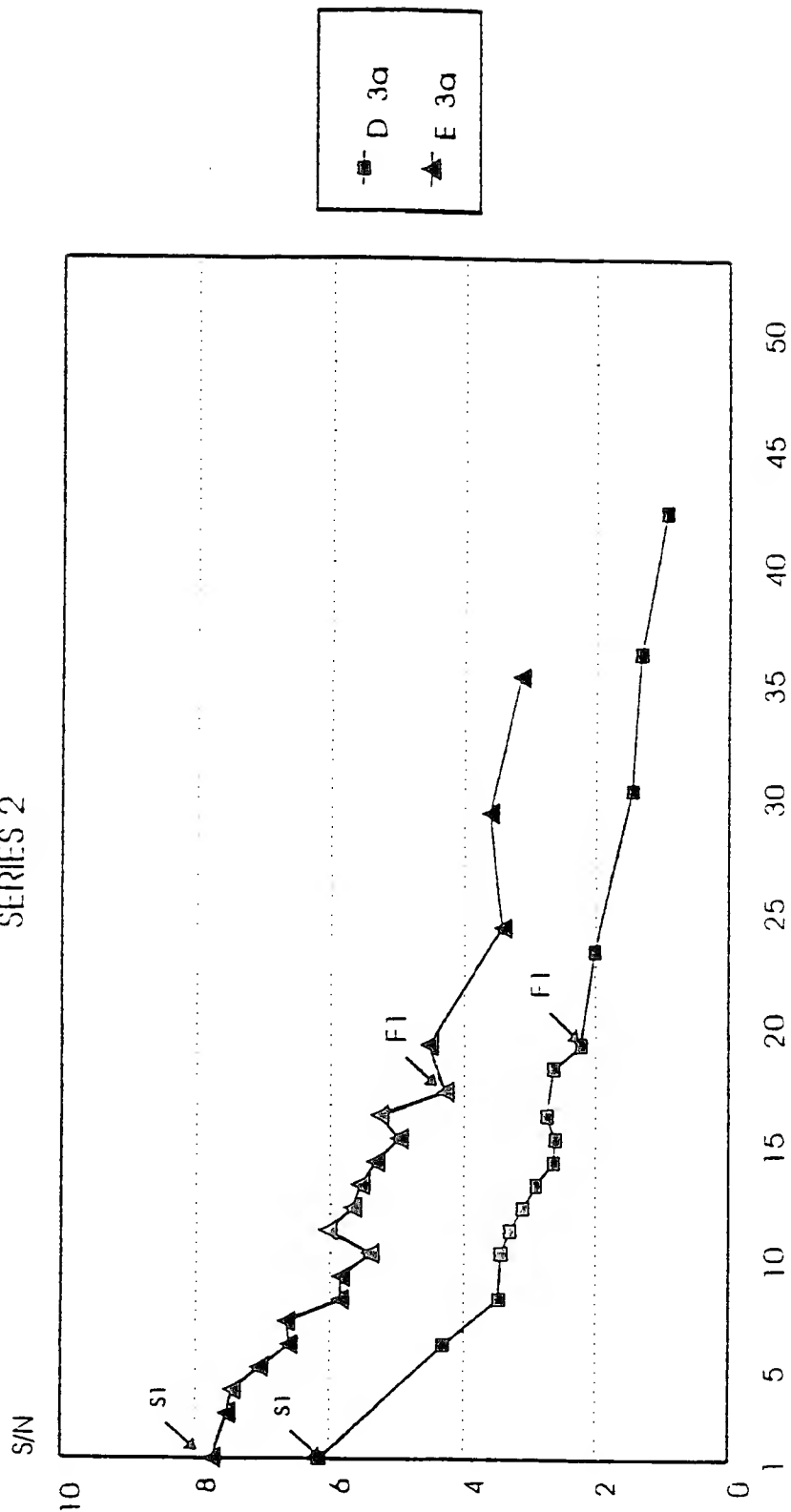


weeks after start of treatment

Fig. 6

Anti-E1 levels in patients with COMPLETE response to IFN

SERIES 2

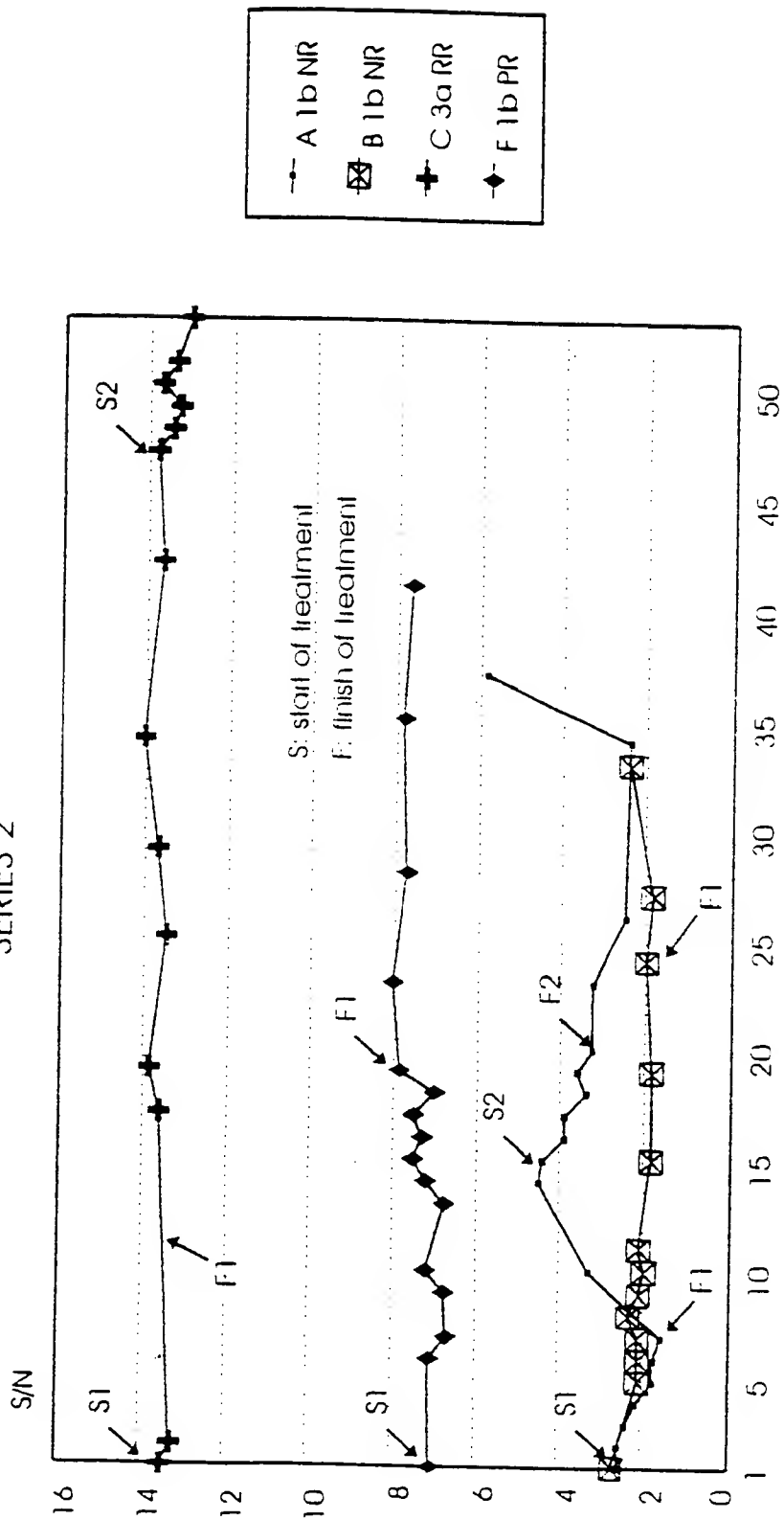


months after start of treatment

Fig. 7

Anti-E1 levels in INCOMPLETE responders to IFN treatment

SERIES 2

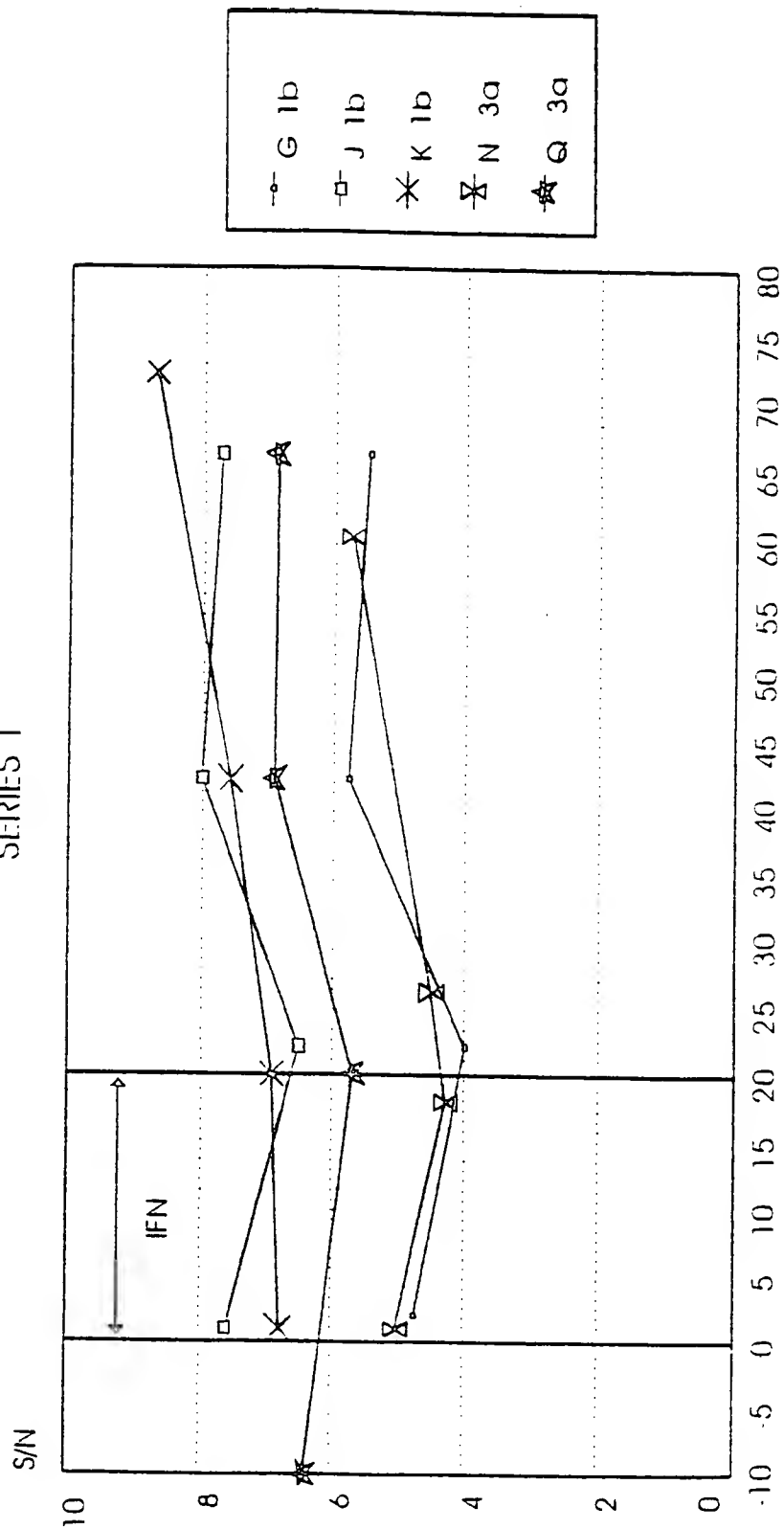


months after start of treatment

Fig. 8

Anti-E2 levels in NON-RESPONDERS to IFN treatment

SERIES 1



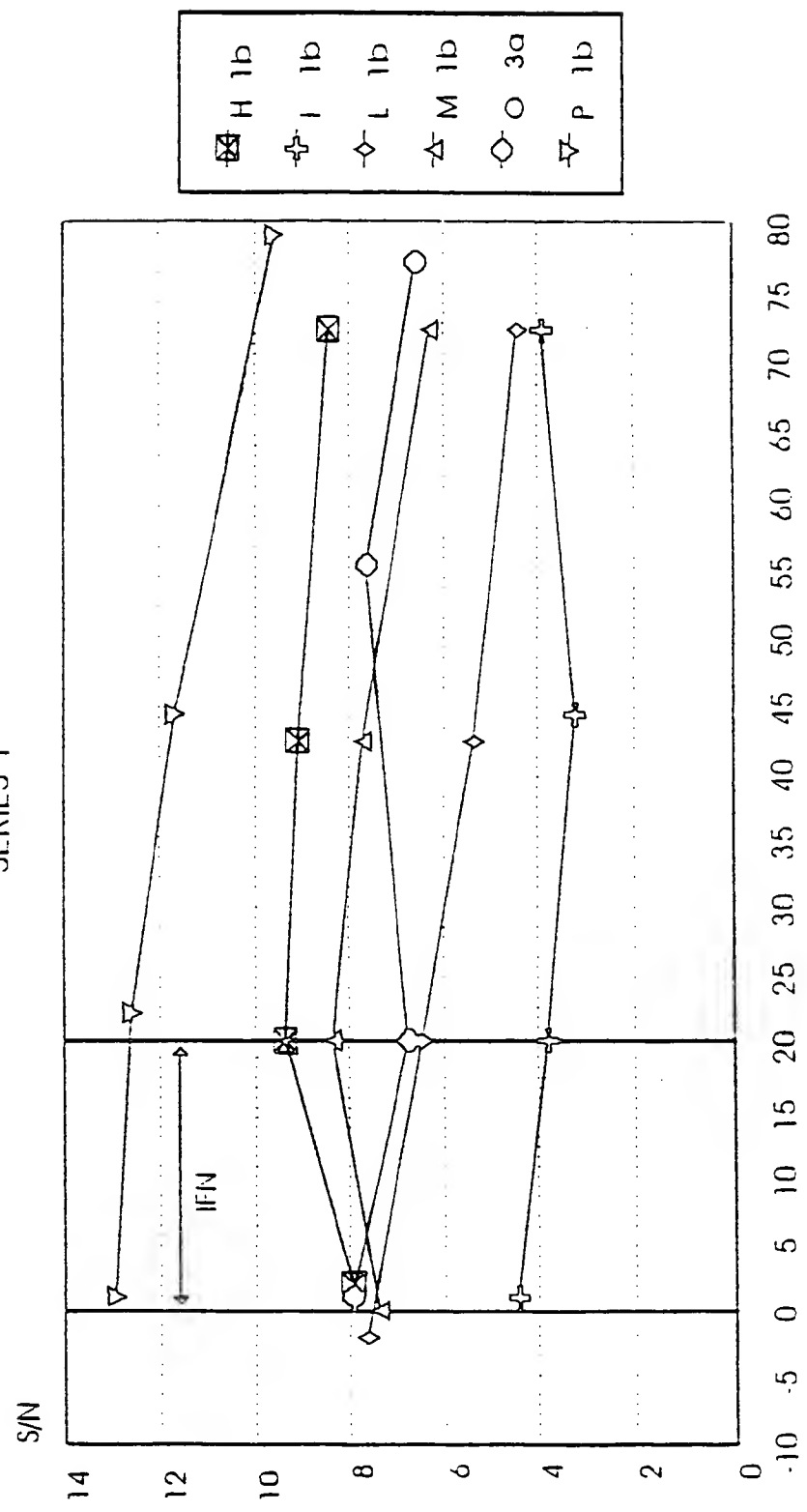
weeks after start of treatment

Fig. 9

FOOTPRINT "0005560

Anti-E2 levels in RESPONDERS to IFN treatment

SERIES 1

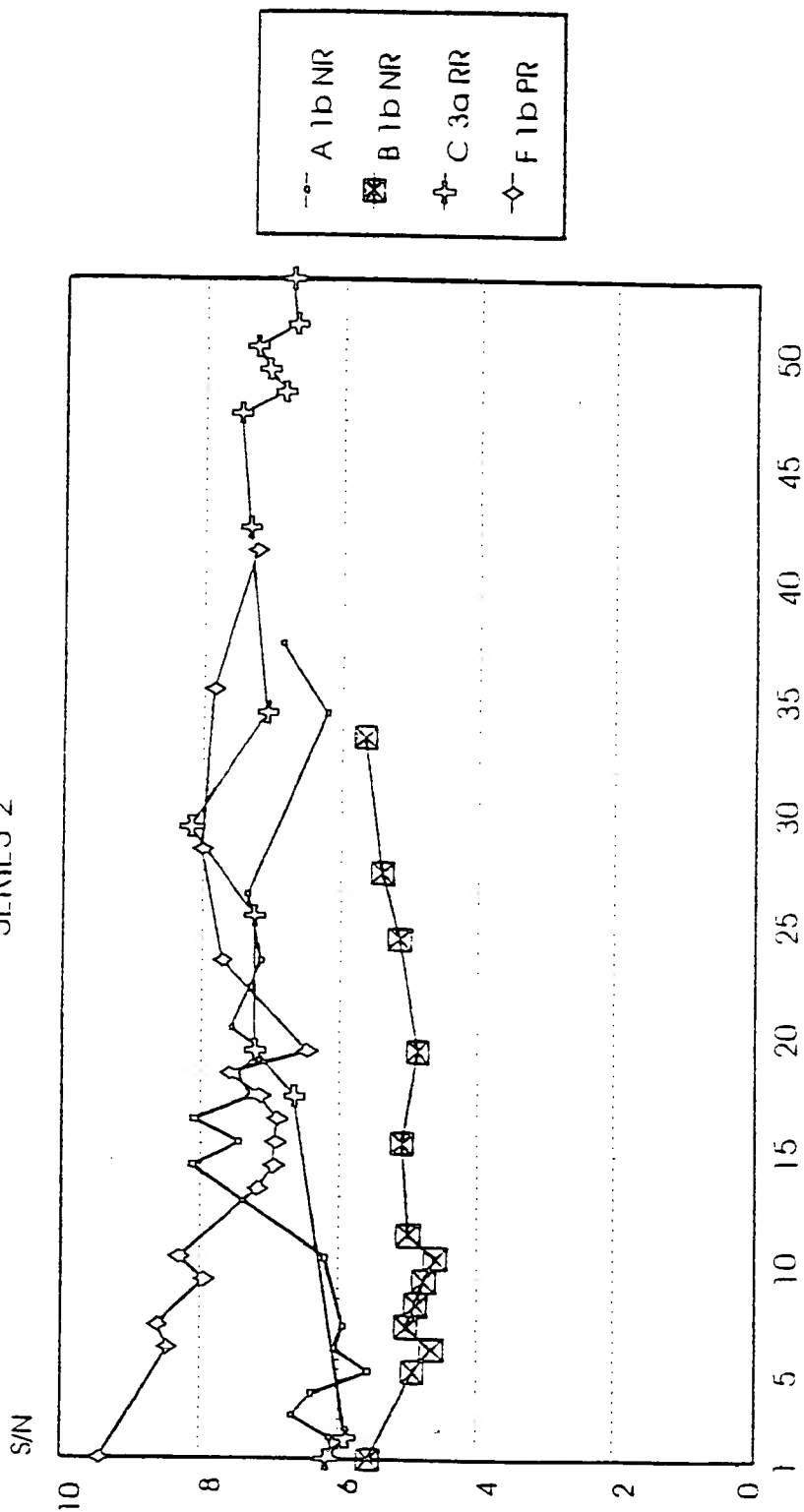


weeks after start of treatment

Fig.10

Anti-E2 levels in INCOMPLETE responders to IFN treatment

SERIES 2



months after start of treatment

Fig.11

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Human anti-E1 reactivity competed with peptides

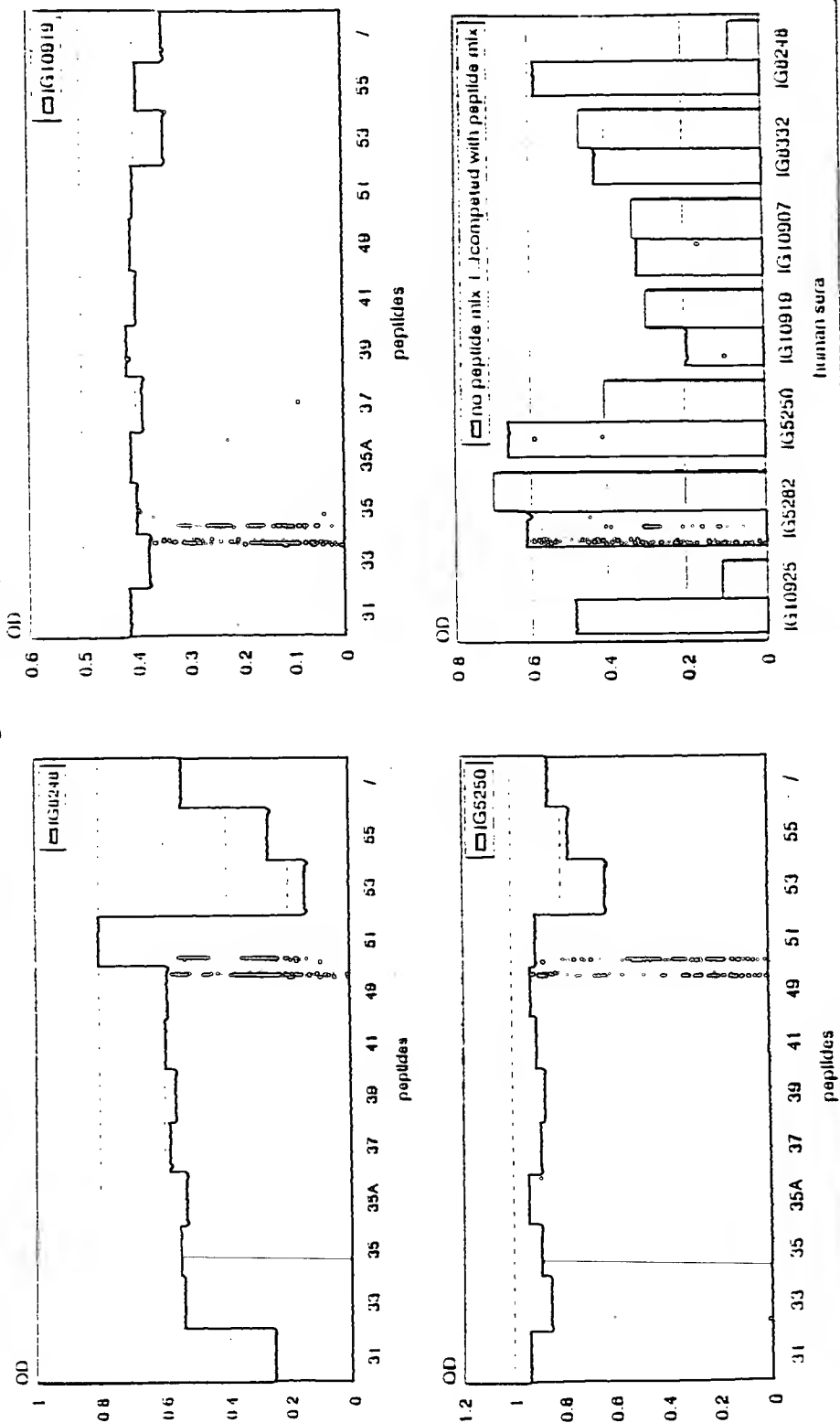


Fig.13

Competition of reactivity of anti-E1 Mabs with peptides

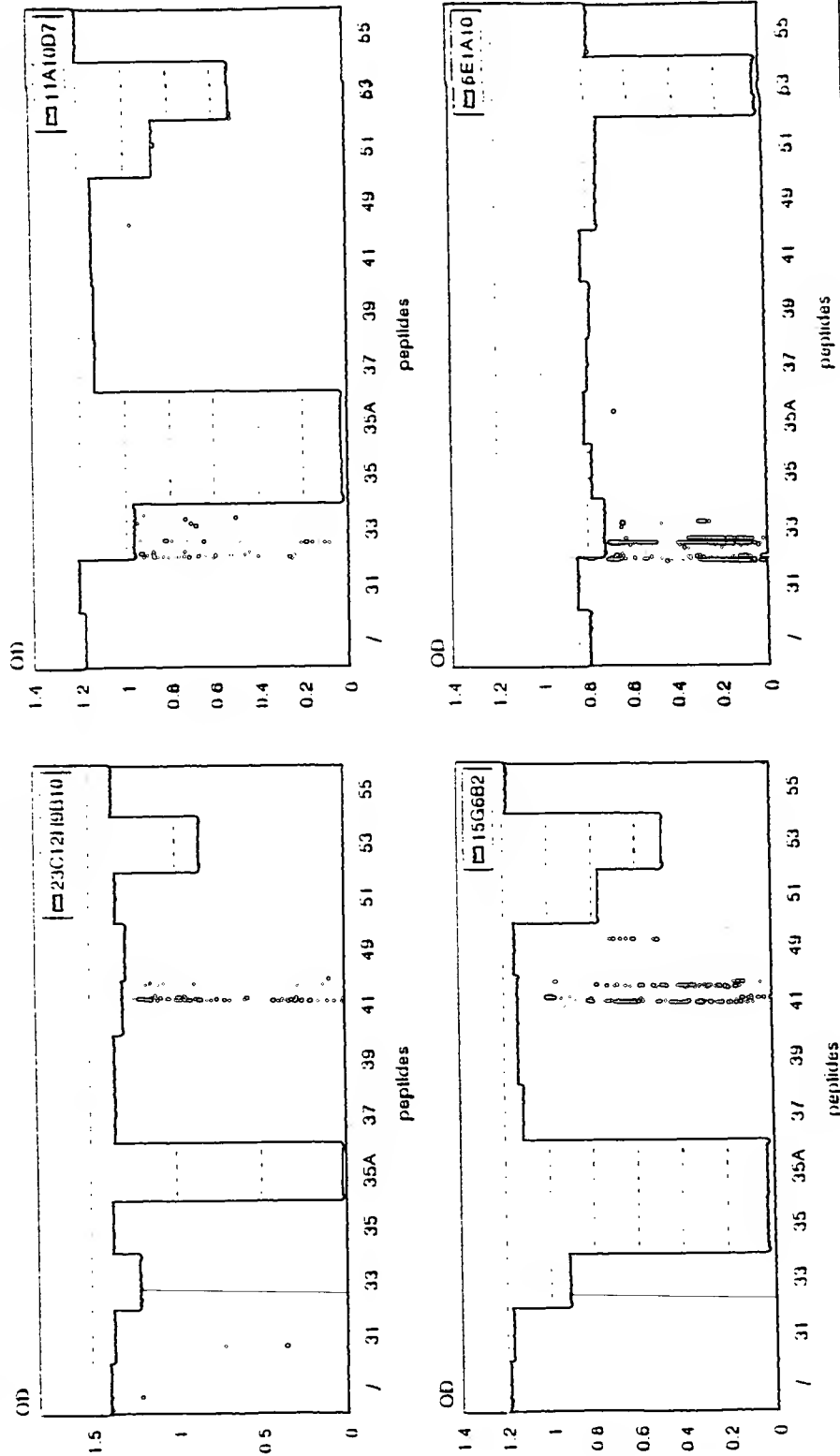
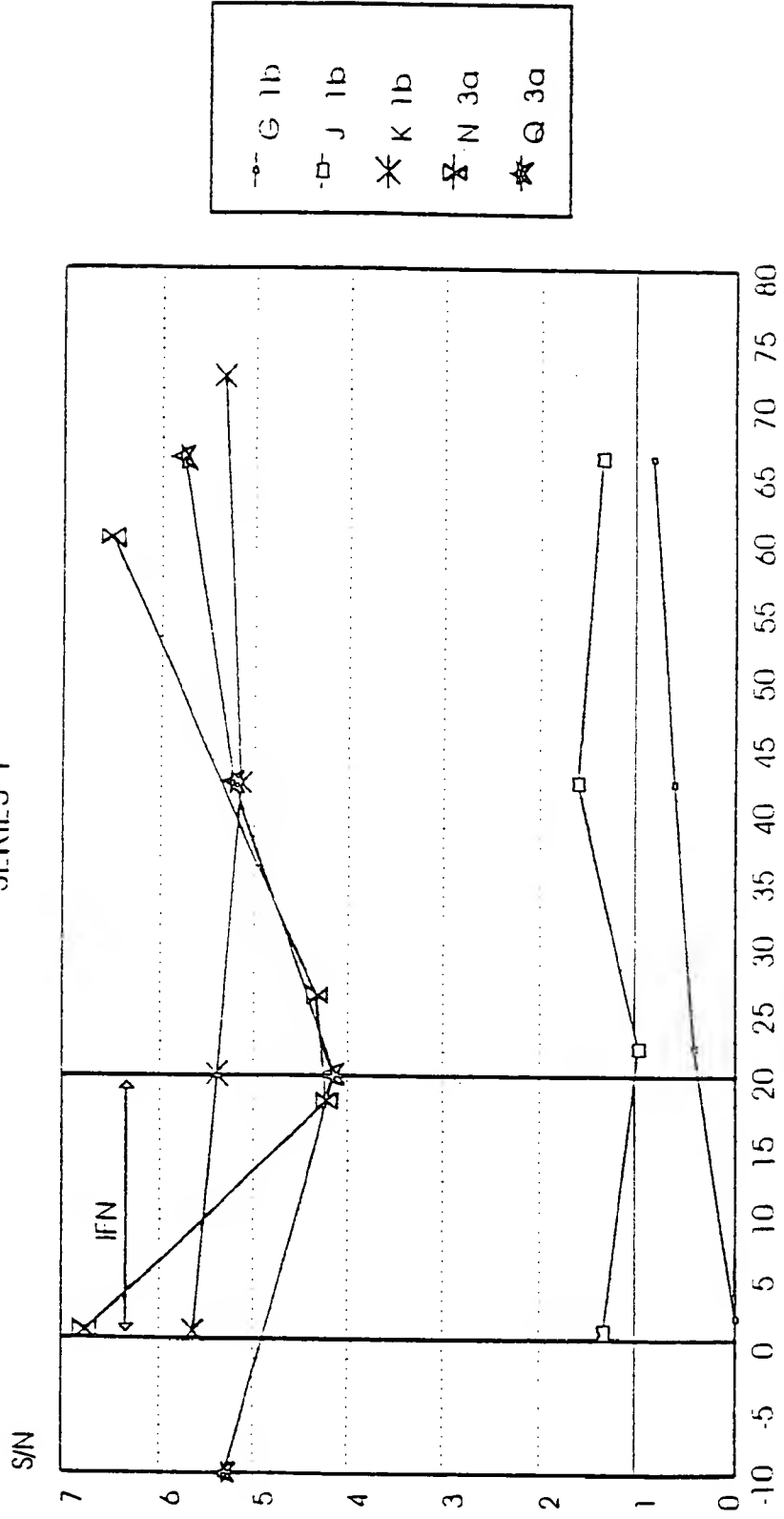


Fig.14

Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment

SERIES 1



weeks after start of treatment

Fig.15

Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

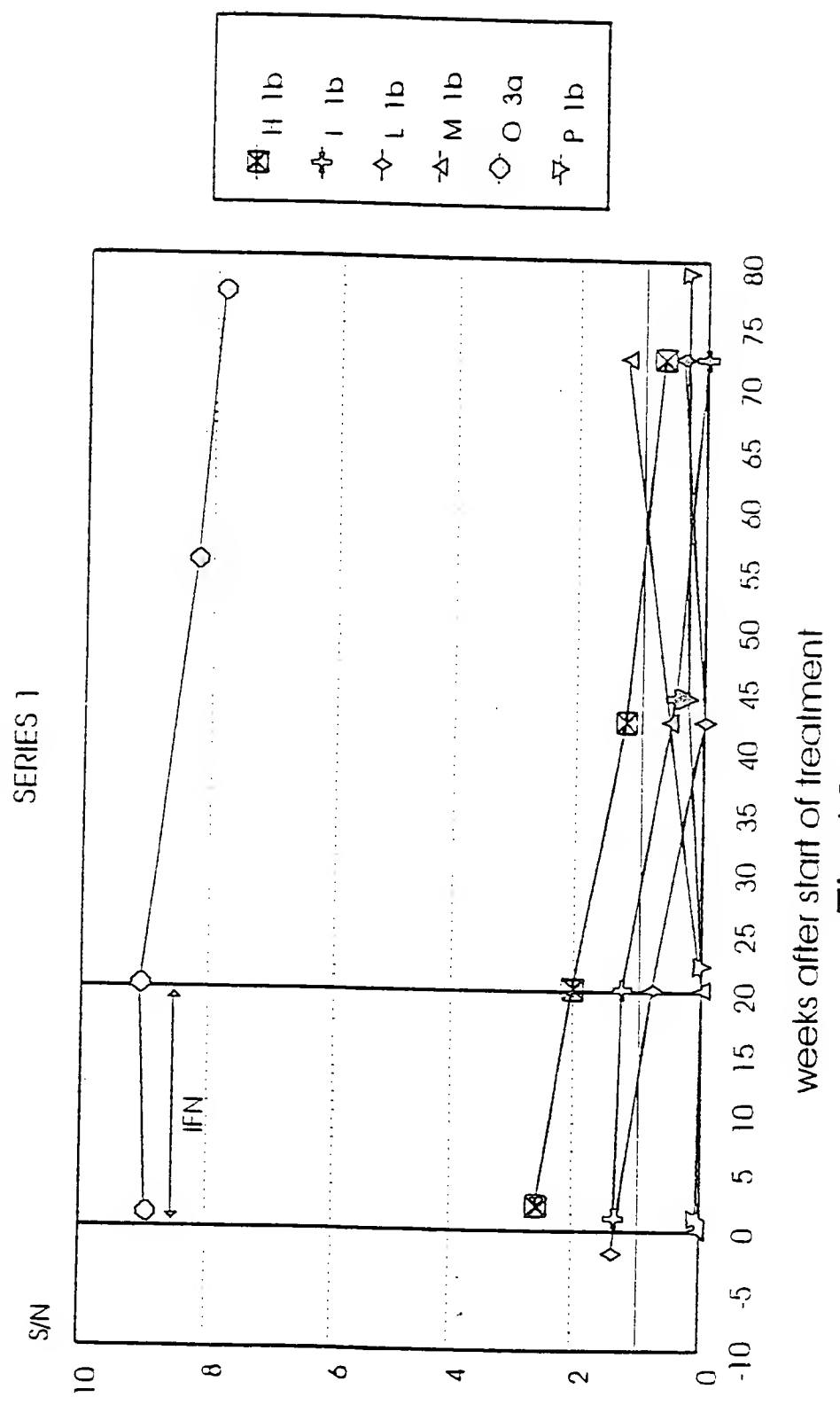


Fig.16

Anti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment

SERIES 1

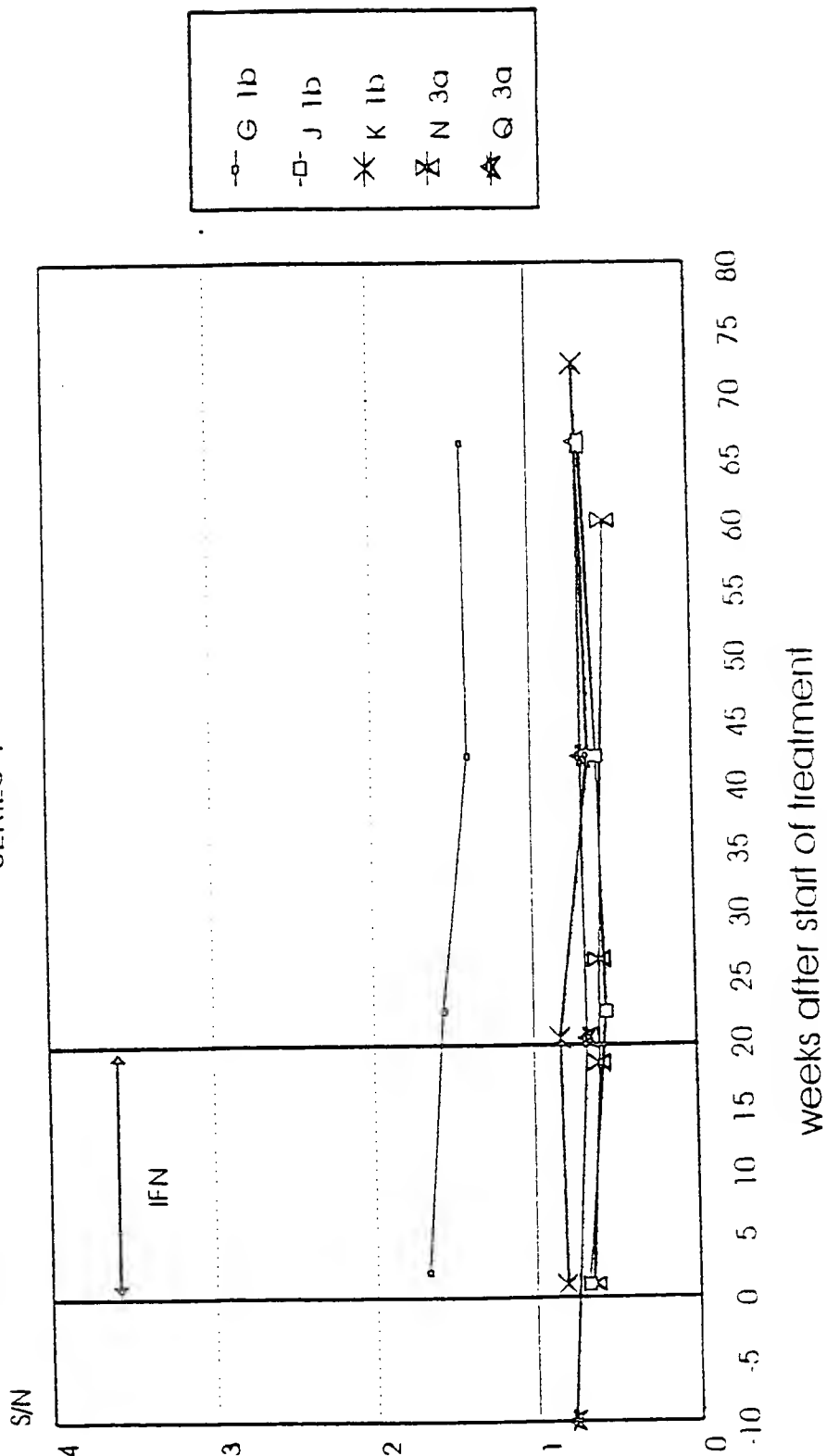
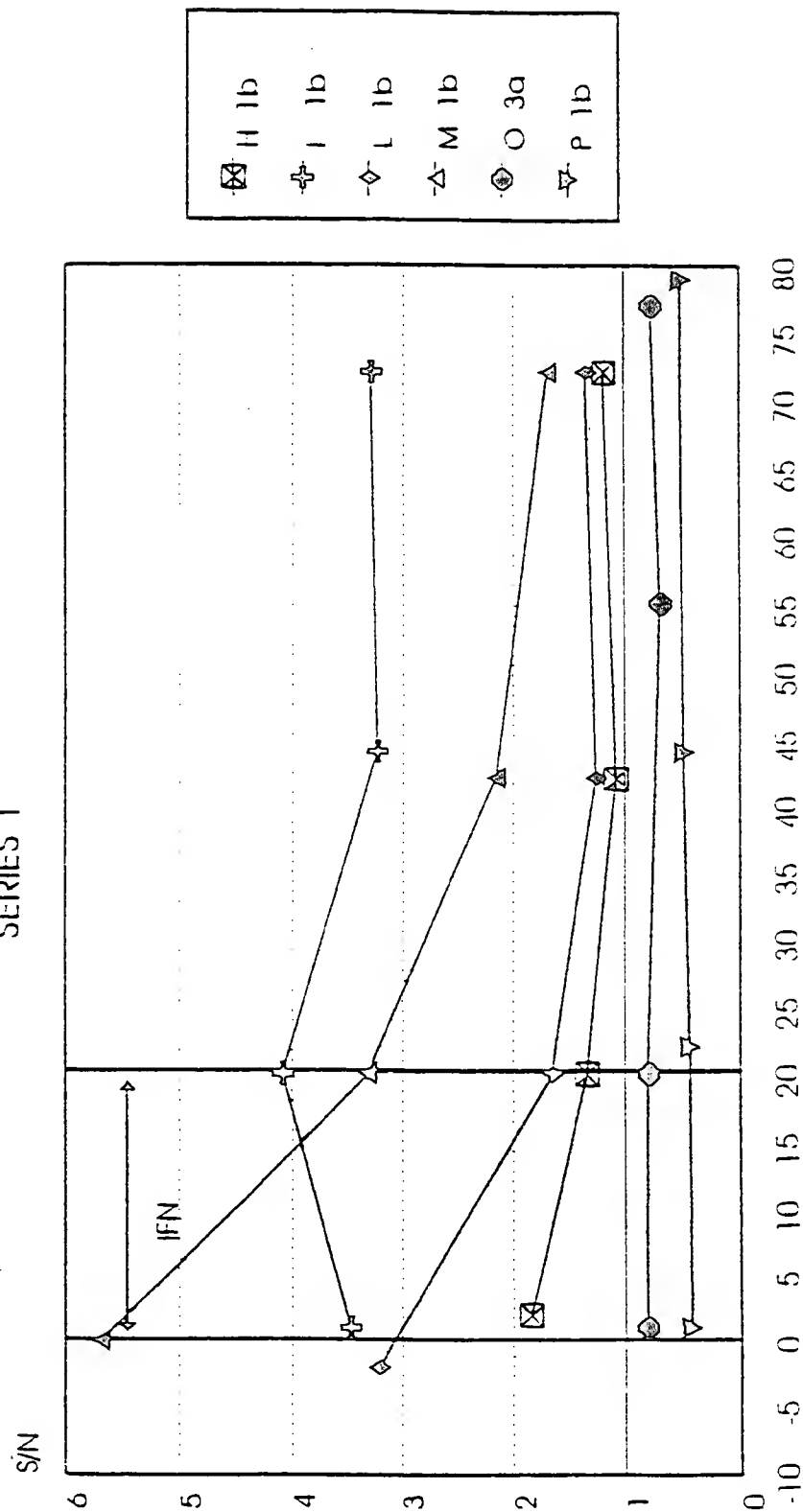


Fig.17

Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

SERIES 1



weeks after start of treatment

Fig.18

Competition of reactivity of anti-E2 Mabs with peptides

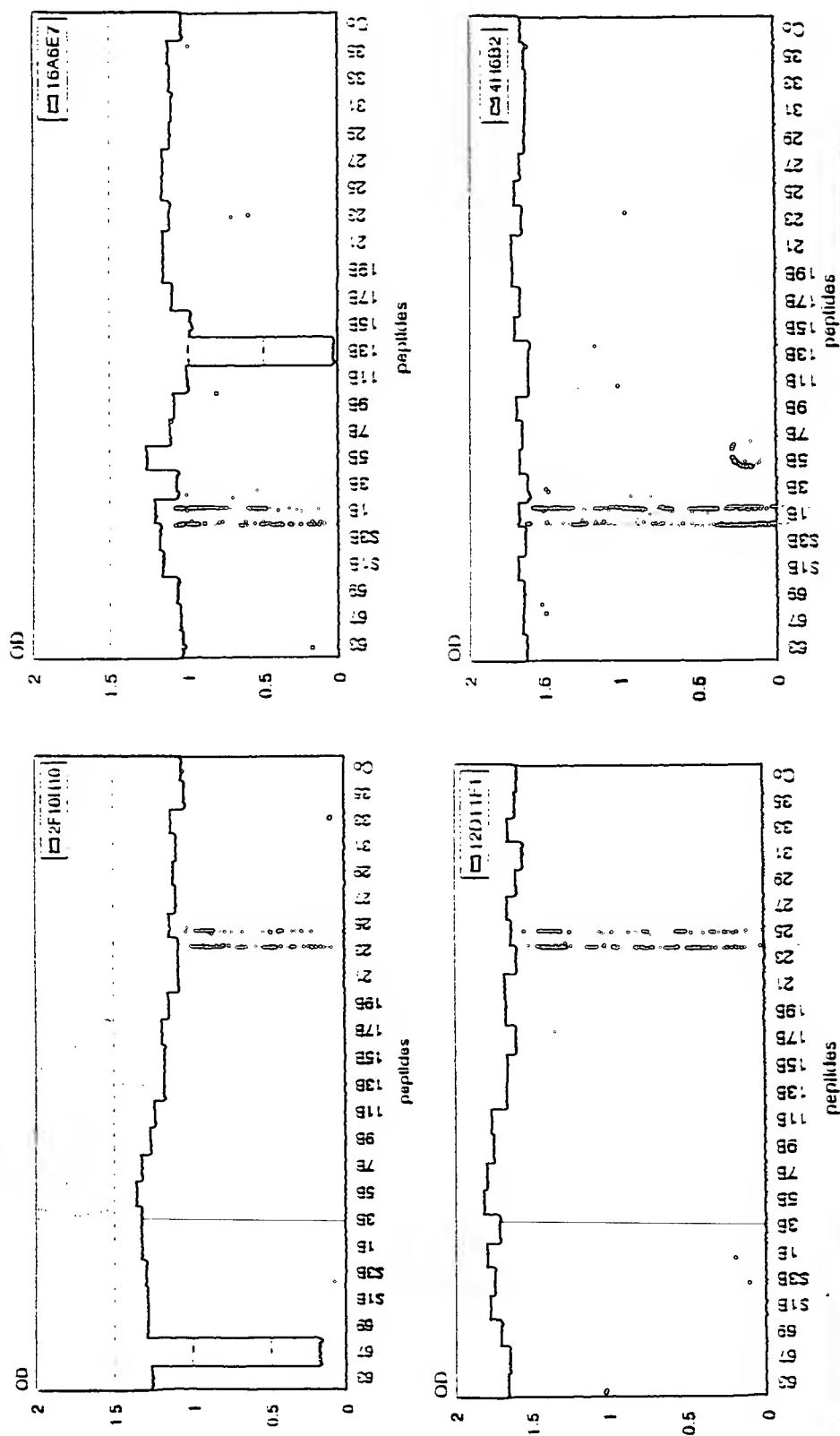


Fig.19

Human anti-E2 reactivity competed with peptides

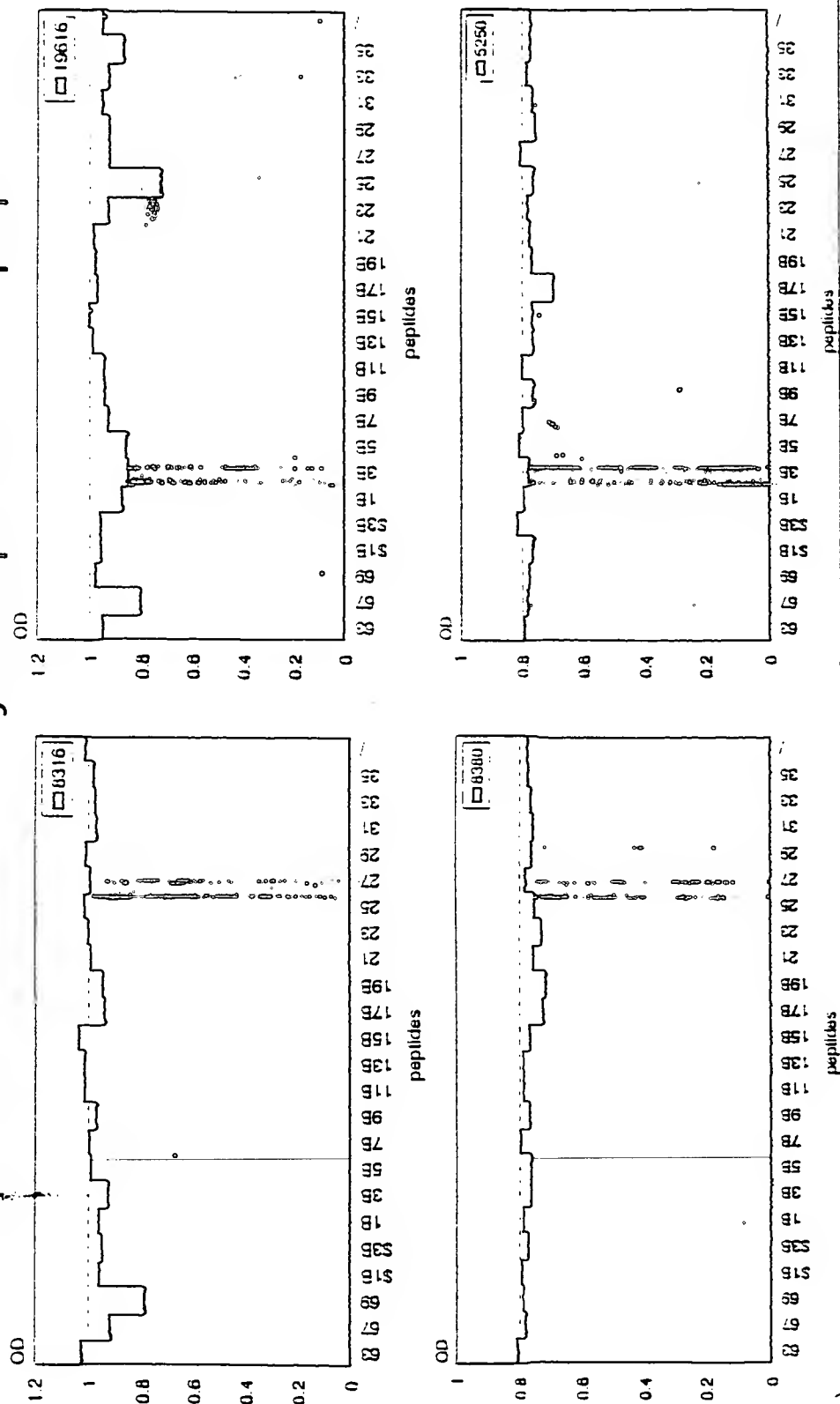


Fig. 20

5

3'ACGTC CGTACGTT CGAATTAATTAATCGA5' (SEQ ID NO 94)

3' CCTCCGGACGTGCACTAGCTCCCGTCTGTGGTAGTGGTGGTAGTGATTATCAATTAAATTG
5' (SEQ ID NO 95)

ATGCCCGGTTGCTCTTTCTCTATCTTCCTCTTGGCTTACTGTCTGTCTGACCAATTCAG
GCTTCCGCTTATGAGGTGCGCAACGTGTCCGGGATGTACCATGTACGAAACGACTGCT
CCAACTCAAGCATTGTGTATGAGGCAGCGGACATGATCATGCACACCCCCCGGTGCGT
GCCCTGCGTTCCGGGAGAACAACCTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTC
GCAGCTAGGAACGCCAGCGTCCCCACCACGACAATACGACGCCACGTCTGATTTGCTCG
TTGGGGCGGGCTGCTCTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTC
CTCGTCTCCCAGCTGTTCACCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCA
ATTGCTCAATCTATCCCGGCCACATAACAGGTACCGTATGGCTTGGGATATGATGAT
GAACTGGTCGCCTACAACGGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCCACAAGCT
GTCGTGGACATGGTGGCGGGGGCCCAATTGGGGAGTCCTGGCGGGCCTCGCCTACTATT
CCATGGTGGGGAACCTGGGCTAAGGTTTTGATTGTGATGCTACTCTTTGCTCTCTAATAG

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GGTTCCTGGAGGACGGCGTGAACATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT
ATCTTCCTCTTGGCTTTGCTGTCTGTGACCGTTCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCCAACCTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAAC
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TCCCCACCACGACAATACGACGCCACGTGATTTGCTCGTTGGGGCGGCTGCTTTCTG

[illegible]

[illegible]

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Fig. 21C

GCCCTGCGTTCCGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTC
GCGGCCAGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTGCAATTTGCTC
GTTGGGGCTGCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTT
CCTTGTTTTCCAGCTGTTTACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCA
ACTGCTCAATCTATCCCGGCCATGTATCAGGTCAACGCATGGCTTGGGATATGATGAT
GAACTGGTAATAG

SEQ ID NO 13 (HCC17A)

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GGTTCTGGAAGACGGCGTGAACATGCAACAGGGAATTTGCCTGGTTGCTCTTTCTCTA
TCTTCTCTTTGGCTTTACTGTCTGTCTAACCATTCAGCTTCCGCTTACGAGGTGCGC
AACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATG
AGGCAGCGGACATGATCATGCACACCCCGGGTGCCTGCCCTGCGTTCCGGGAGAACA
ACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCGGCTAGGAACGCCAGCAT
CCCCACTACAACAATACGACGCCACGTGCAATTTGCTCGTTGGGGCGGCTGCTTTCTGTT
CGGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTCTCTCGTCTCCAGCTGTTTACC
ATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCC
ACATAACGGGTCAACGCTATGGCTTGGGATATGATGATGAACTGGTACTAATAG

SEQ ID NO 15 (HCP151)

ATGCCCGGTTGCTCTTTCTCTATCTT

SEQ ID NO 16 (HCP152)

ATGTTGGGTAAAGGTCATCGATACCCT

SEQ ID NO 17 (HCP153)

CTATTAGGACCAGTTCATCATCATATCCCA

SEQ ID NO 18 (HCP154)

CTATTACCAGTTCATCATCATATCCCA

SEQ ID NO 19 (HCP107)

ATACGACGCCACGTGCAATTCAGCTGTTTACCATC

Fig. 21D

SEQ ID NO 20 (HCP108)

GATGGTGAACAGCTGGGAATCGACGTGGCGTCGTAT

SEQ ID NO 21 (HCC137)

ATGTTGGGTAAGGTCATCGATACCCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACA
TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT
ATCTTCCTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGGC
CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAAC
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TCCCCACCAACGACAATACGACGCCACGTGCGATTCCCAGCTGTTCAACCATCTCGCCTCG
CCGGCATGAGACCGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT
CACCGTATGGCTTGGGATATGATGATGAACTGGTCCCTACAACGGCCCTGGTGGTAT
CGCAGCTGCTCCGGATCCACAAAGCTGTCTGGACATGGTGGCGGGGGGCCATTGGGG
AGTCTGGCGGGTCTCGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGATTG
TGATGCTACTCTTTGCTCCCTAATAG

SEQ ID NO 23 (HCC138)

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TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT
ATCTTCCTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGGC
CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAAC
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TCCCCACCAACGACAATACGACGCCACGTGCGATTCCCAGCTGTTCAACCATCTCGCCTCG
CCGGCATGAGACCGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT
CACCGTATGGCTTGGGATATGATGATGAACTGGTAA
TAG

SEQ ID NO 25 (HCC139)

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TTCCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
GGTTCTGGAGGACGGCGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT

Fig. 21E

ATCTTCCTCTTGGCTTTGCTGTCTGTGACCGTTCCAGCTTCCGCTTATGAAGTGCG
CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTAT
GAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGAGAAC
AACTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCG
TCCCCACCACGACAATACGACGCCACGTGCGATTCCCAGCTGTTACCATCTCGCCTCG
CCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGT
CACCGTATGGCTTGGGATATGATGATGAACTGGTGCCTACAACGGCCCTGGTGGTAT
CGCAGCTGCTCCGGATCCTCTAATAG

SEQ ID NO 27 (HCC140)

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TTCCGCTCGTGGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCG
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CAACGTGTCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTAT
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SEQ ID NO 29 (HCC162)

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CGCTCGTCCGGCGCTCCCGTAGGAGGCGTCGCAAGAGCCCTTGCGCATGGCGTGAGGGC
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TCCTTCTCGCTCTGTTCTCTTGCTTAATTCATCCAGCAGCTAGTCTAGAGTGGCGGAAT
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CGATGACGTTATTCTGCACACACCCGGCTGCATACCTTGTGTCCAGGACGGCAATACA
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CCGCTTCGATACGCAGTCATGTGGACCTATTAGTGGGCGCGGCCACGATGTGCTCTGC
GCTCTACGTGGGTGACATGTGTGGGGCTGTCTTCCTCGTGGGACAAGCCTTACGTTCA
GACCTCGTCCCATCAAACGGTCCAGACCTGTAACCTGCTCGCTGTACCCAGGCCATCT
TTCAGGACATCGAATGGCTTGGGATATGATGATGAACTGGTAATAG

FIG. 21E

[illegible]

TGGGATATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCC
GGATCCCACAAGCTGTGCTGGACATGGTGGCGGGGGGCCCAATTGGGGAGTCCTGGCGG
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GGGGCCCTTGTGTCCCTCTTTAGCCCCGGGTGGGCTCAGAAAATCCAGCTCGTAAACAC
CAACGGCAGTTGGCACAACAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAAC
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CGACTCGGATGTGCTGATTCTCAACAACACGCGGCCGCGCGAGGCAACTGGTTCGGC
TGTACATGGATGAATGGCACTGGGTTACCAAGACGTGTGGGGGGCCCCCGTGCAACA
TCGGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCC
CGAGGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTT

[illegible]

SEQ ID NO 37 (HCC141)

SEQ ID NO 39 (HCCI42)

GATCCGACAAGCTGTCGTGGACATGGTGGCGGGGGCCATTGGGGAGTCCTGGCGGG
CCTCGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGTTGTGATGCTACTCT

$\frac{d}{dt} \left(\frac{1}{r^2} \right) = -\frac{2}{r^3} \frac{dr}{dt}$

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1. *Phragmites australis* (Cav.) Trin. ex Steud.
 2. *Spartina patens* (Muhl.) B. & P.
 3. *Scirpus americanus* (L.) Pers.
 4. *Distichlis spicata* (L.) Nees
 5. *Eleocharis acicularis* (L.) Rostk Schmidt
 6. *Eleocharis obtusa* (L.) Nees
 7. *Eleocharis palustris* (L.) Rostk Schmidt
 8. *Eleocharis acicularis* (L.) Rostk Schmidt
 9. *Eleocharis obtusa* (L.) Nees
 10. *Eleocharis palustris* (L.) Rostk Schmidt
 11. *Eleocharis acicularis* (L.) Rostk Schmidt
 12. *Eleocharis obtusa* (L.) Nees
 13. *Eleocharis palustris* (L.) Rostk Schmidt
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 15. *Eleocharis obtusa* (L.) Nees
 16. *Eleocharis palustris* (L.) Rostk Schmidt
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 19. *Eleocharis palustris* (L.) Rostk Schmidt
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 21. *Eleocharis obtusa* (L.) Nees
 22. *Eleocharis palustris* (L.) Rostk Schmidt
 23. *Eleocharis acicularis* (L.) Rostk Schmidt
 24. *Eleocharis obtusa* (L.) Nees
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 27. *Eleocharis obtusa* (L.) Nees
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 99. *Eleocharis obtusa* (L.) Nees
 100. *Eleocharis palustris* (L.) Rostk Schmidt

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[illegible]

—

[illegible]

1. 4000

Fig. 21L

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TGTGGCCGCTGCTCCTGCTTCTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAA

TCGGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAACAGGACT

Fig. 22

OD measured at 450 nm
construct

Fraction	volume	dilution	39 Type 1b	40 Type 1b	62 Type 3a	63 Type 3a
START	23 ml	1/20	2.517	1.954	1.425	1.142
FLOW THROUGH	23 ml	1/20	0.087	0.085	0.176	0.120
1	0.4 ml	1/200	0.102	0.051	0.048	0.050
2			0.396	0.550	0.090	0.067
3			2.627	2.603	2.481	2.372
4			3	2.967	3	2.694
5			3	2.310	2.640	2.154
6			2.694	2.499	1.359	1.561
7			2.408	2.481	0.347	1.390
8			2.176	1.970	1.624	0.365
9			1.461	1.422	0.887	0.604
10			1.236	0.926	0.543	0.519
11			0.981	0.781	0.294	0.294
12			0.812	0.650	0.249	0.199
13			0.373	0.432	0.239	0.209
14			0.653	0.371	0.145	0.184
15			0.441	0.348	0.151	0.151
16			0.321	0.374	0.098	0.106
17			0.525	0.186	0.099	0.108
18			0.351	0.171	0.083	0.090
19			0.192	0.164	0.084	0.087

10

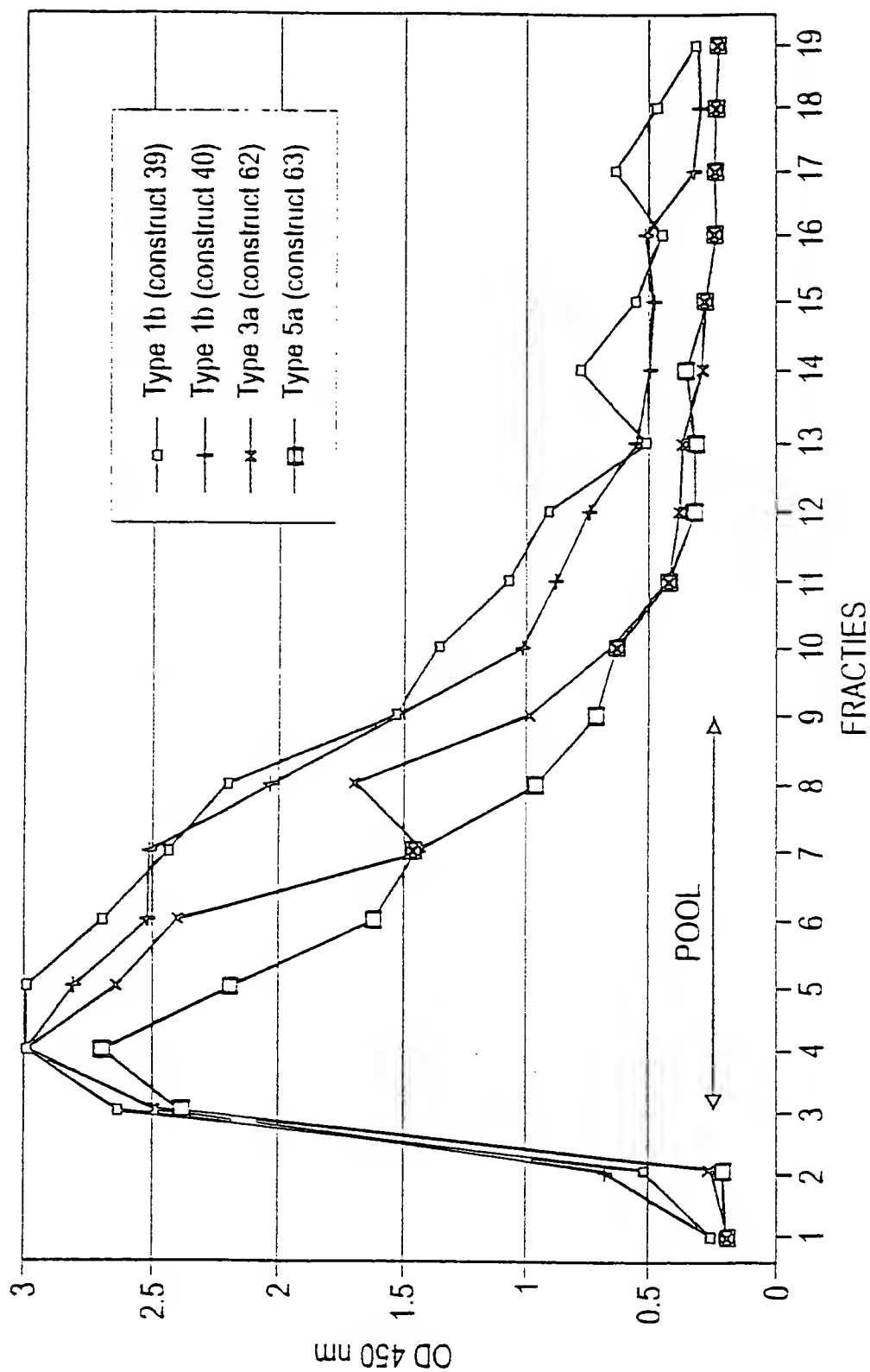


Fig. 23

Figure 24

Fraction	volume	dilution	OD measured at 450 nm			
			construct			
			39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 μ l	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.266	0.438	0.056
25			0.25	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.626	0.889
28			3	3	3	2.345
29			3	3	2.849	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.07	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

100

FO5211-0956660

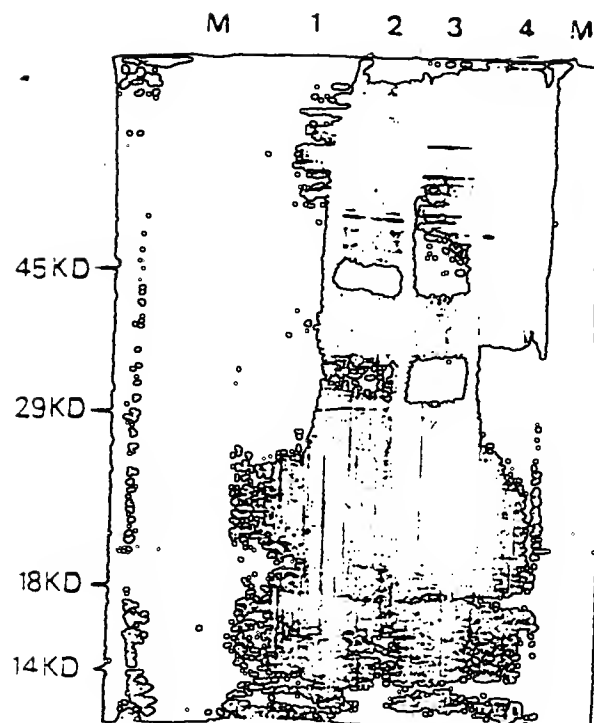


Fig.26

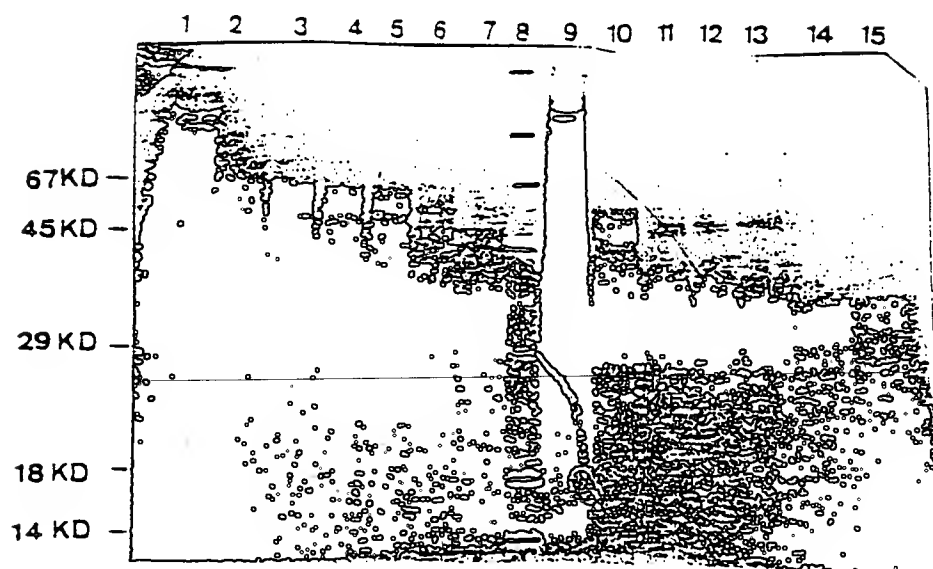


Fig.27

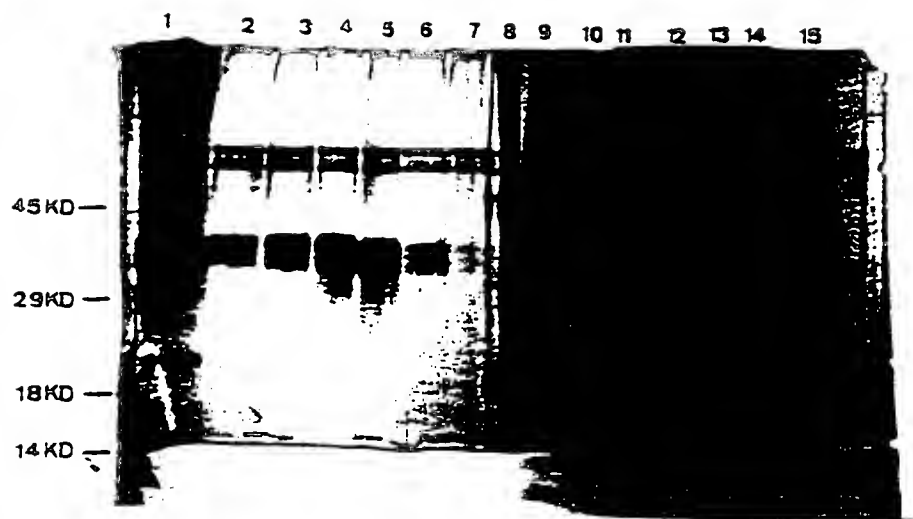


Fig.28

M 1 2 3 4 5 6

Fig.29

67 kD -

45 kD -

29 kD -

18 kD -

14 kD -

- Lane 1: Crude Lysate
- Lane 2: Flow through Lentil Chromatography
- Lane 3: Wash with EMPIGEN Lentil Chromatography
- Lane 4: Eluate Lentil Chromatography
- Lane 5: Flow through during concentration lentil eluate
- Lane 6: Pool of E1 after Size Exclusion Chromatography

000000-4594
000000-000000

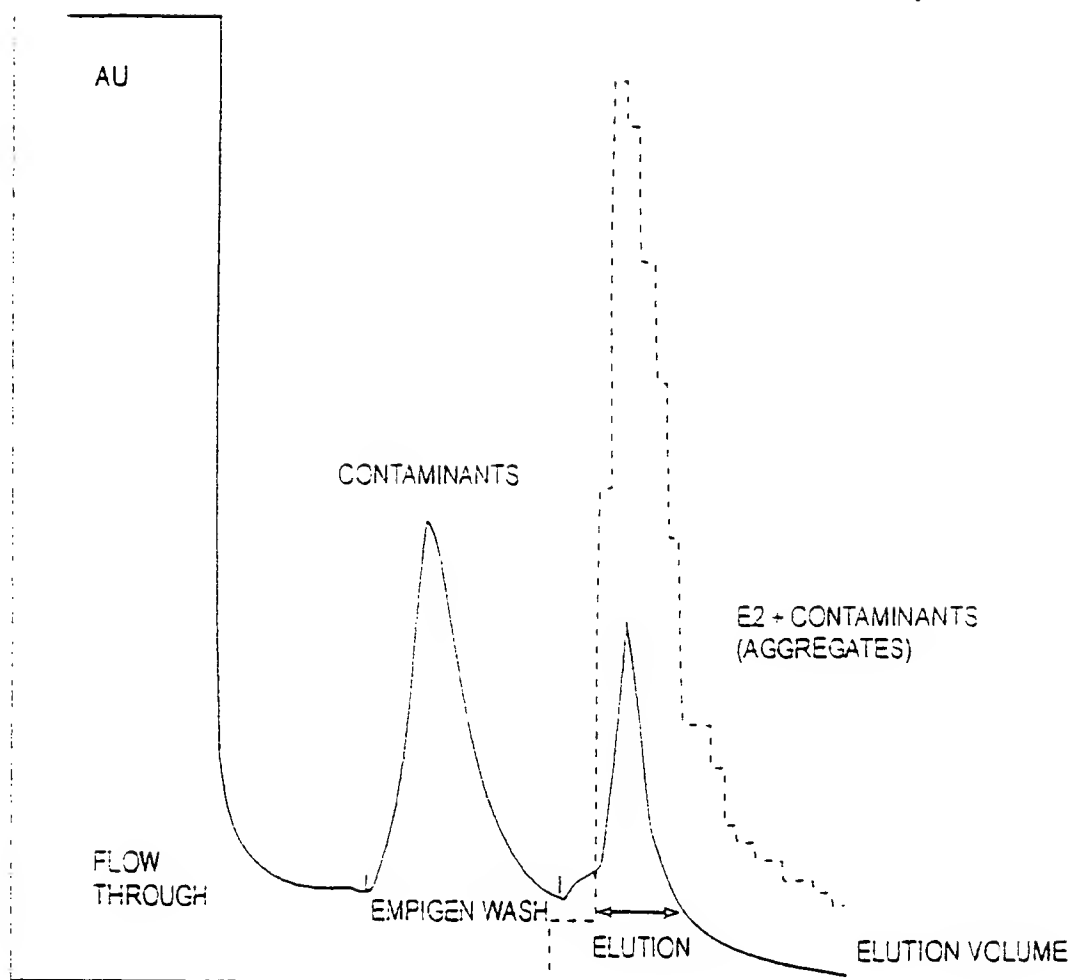
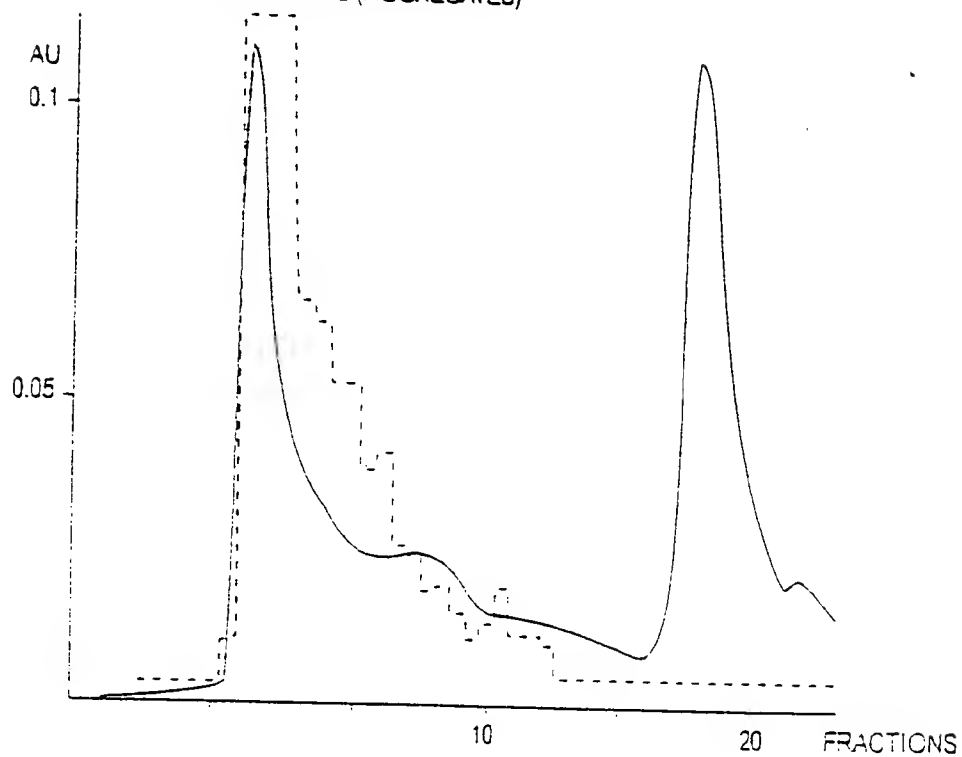


Fig. 30

NON - REDUCED

Fig. 31A

E2 + CONTAMINANTS (AGGREGATES)



REDUCED

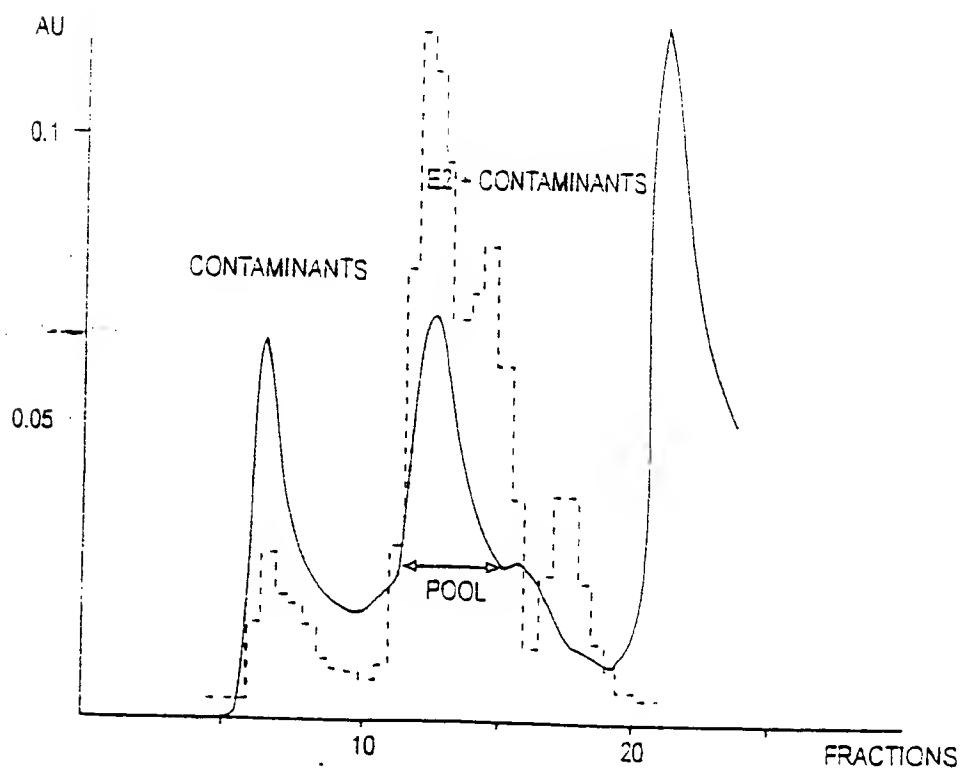


Fig. 31B

406274-03000000

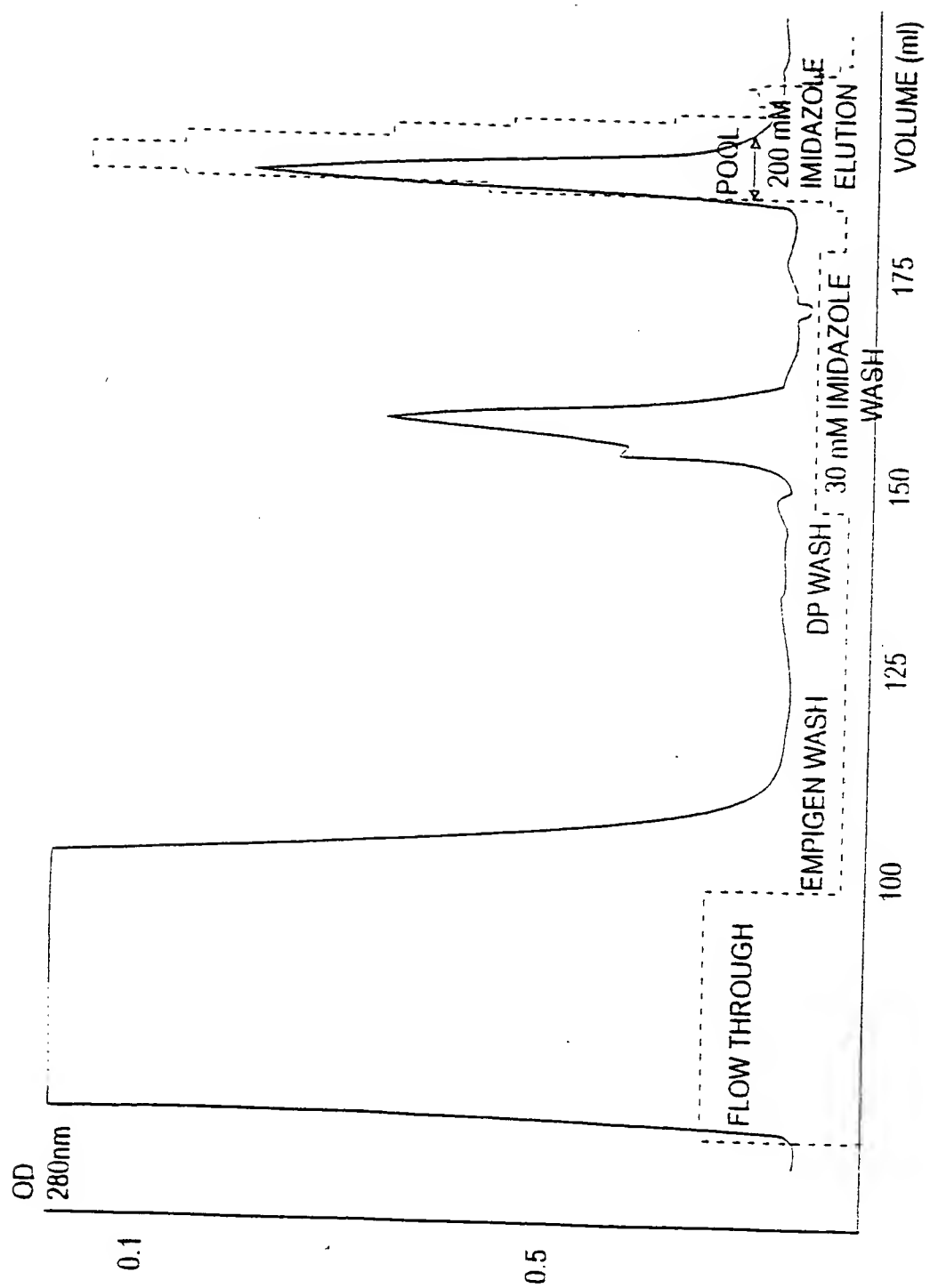
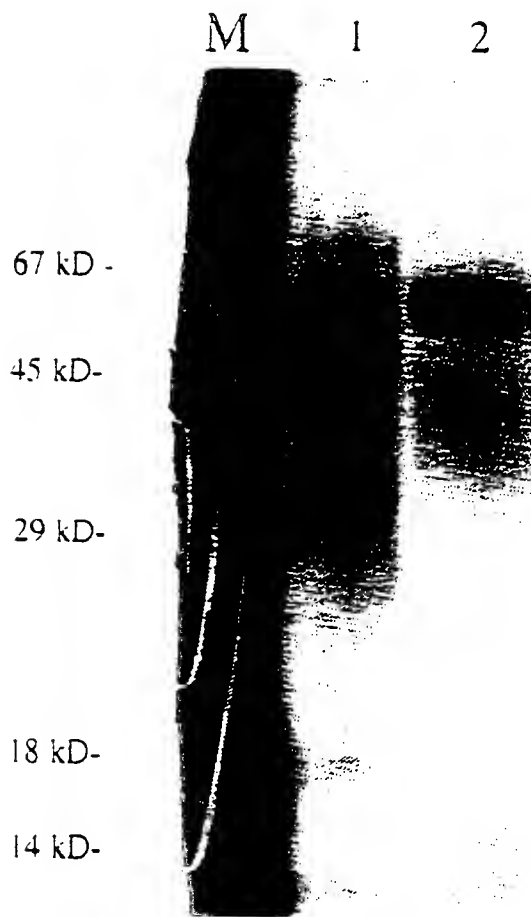


Fig. 32

SILVER STAIN OF PURIFIED E2



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 μ g E2

Fig.33

A histogram showing the distribution of 13 fractions. The x-axis is labeled 'ml' and ranges from 0.0 to 0.3. The y-axis ranges from 0 to 80. The histogram bars are numbered 1 through 13. A dashed curve is overlaid on the histogram, peaking at fraction 5.

Fraction	Approximate Height
1	0
2	5
3	20
4	63
5	88
6	71
7	45
8	25
9	15
10	5
11	0
12	0
13	0

No.	Ret. (min)	Peak start (min)	Peak end (min)	Dur. (min)	Area (min ² mAU)	Height (mAU)
1	0.45	0.46	0.43	0.04	0.0976	4.579
2	1.55	0.75	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.35	3.32	3.35	0.02	0.0002	0.018

Total number of detected peaks = 4
Total Area above baseline = 0.796522 ml*AU
Total area in evaluated peaks = 0.796521 ml*AU
Ratio peak area / total area = 0.999999
Total peak duration = 2.613583 ml

Fig. 34

106277 03052660

NS4 Ab NR

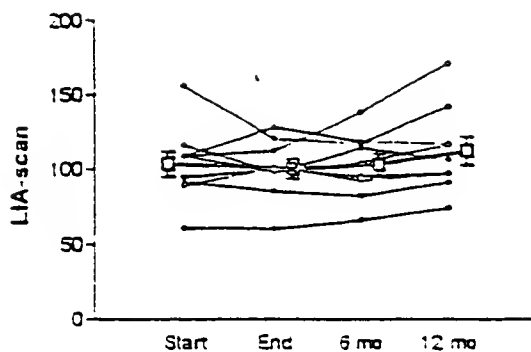


Fig. 35A-1

NS4 Ab LTR

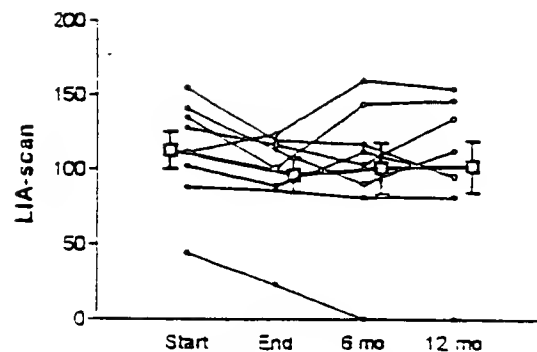


Fig. 35A-2

NS5 Ab NR

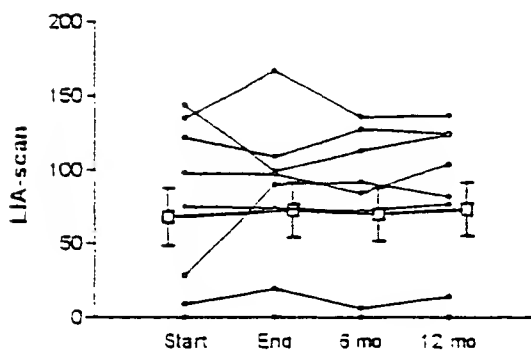


Fig. 35A-3

NS5 Ab LTR

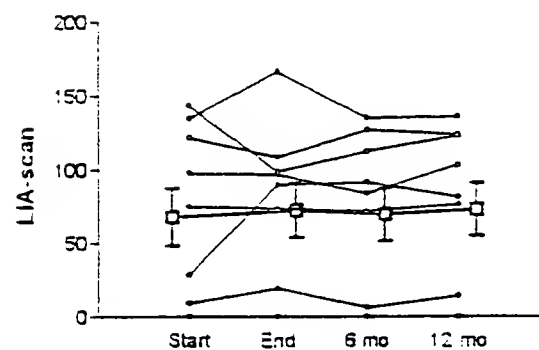


Fig. 35A-4

E1 Ab NR

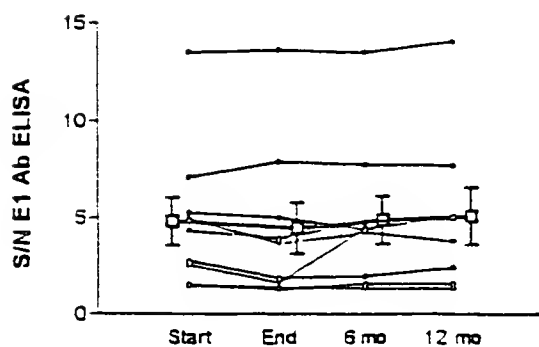


Fig. 35A-5

E1 Ab LTR

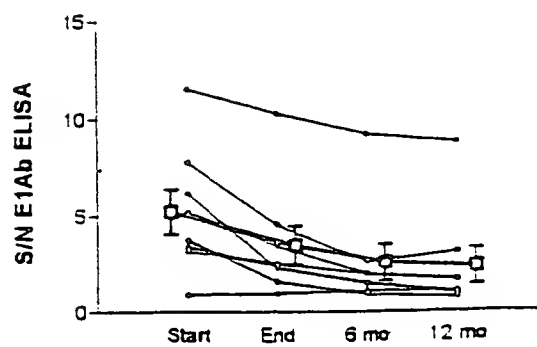
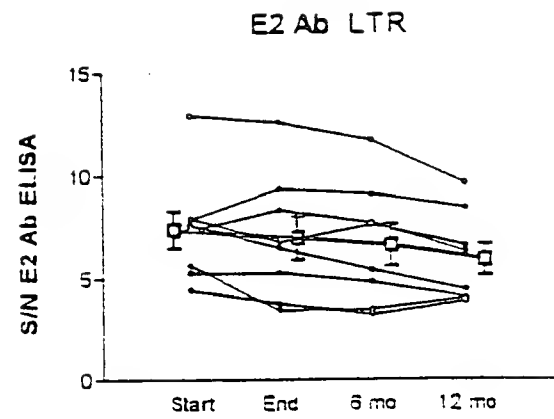
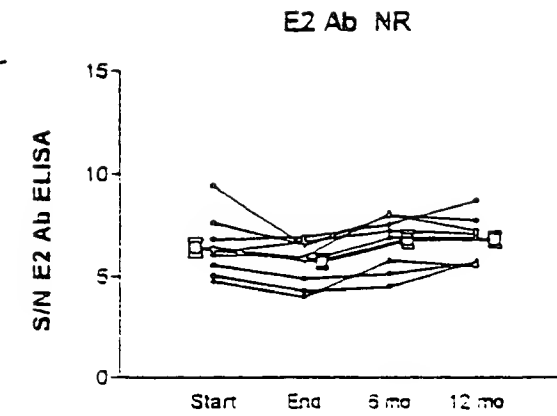


Fig. 35A-6



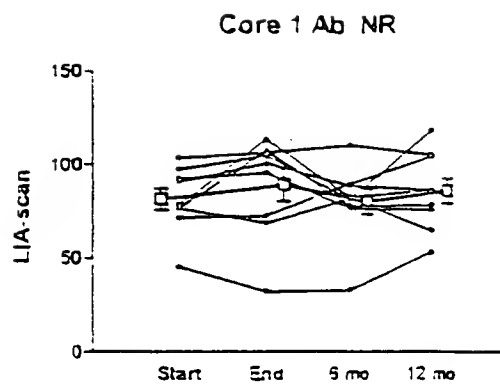


Fig. 35B-1

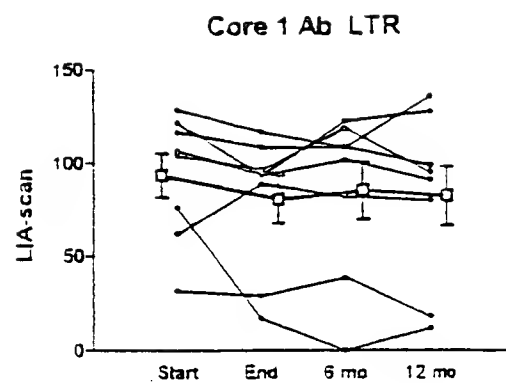


Fig. 35B-2

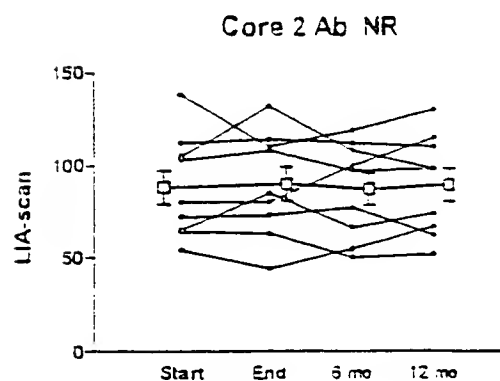


Fig. 35B-3

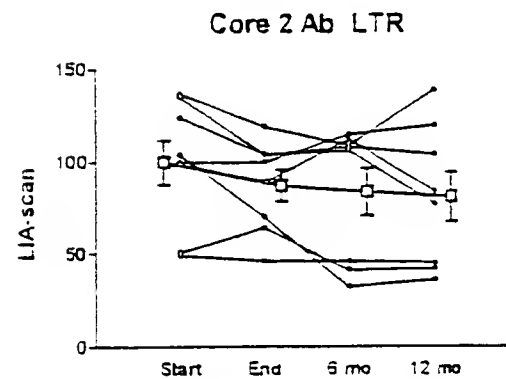


Fig. 35B-4

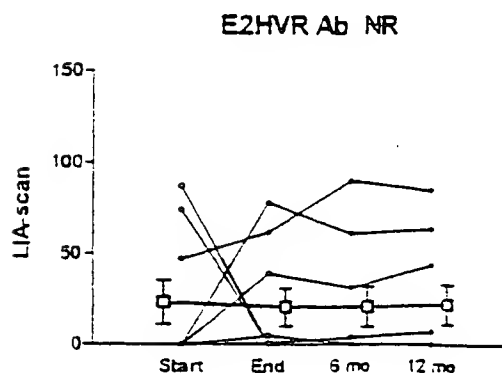


Fig. 35B-5

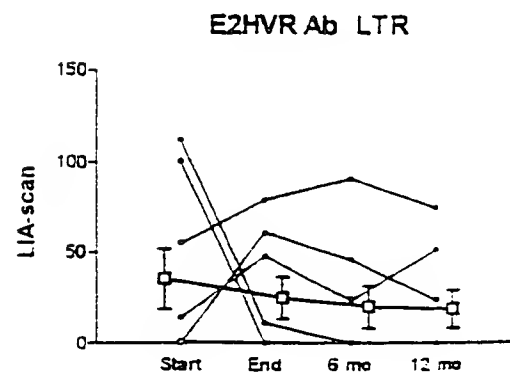


Fig. 35B-6

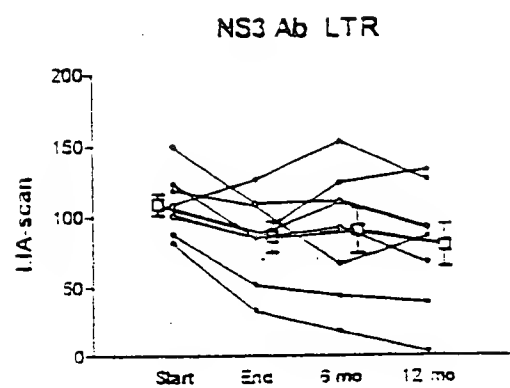
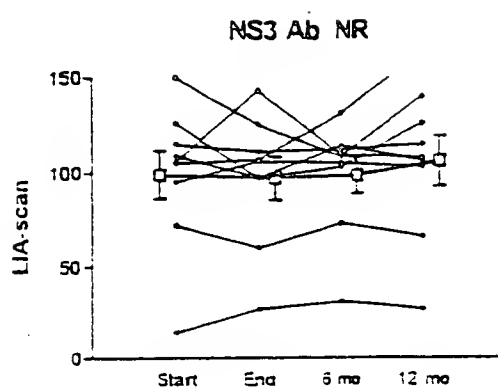


Fig. 36A

E1 Ab

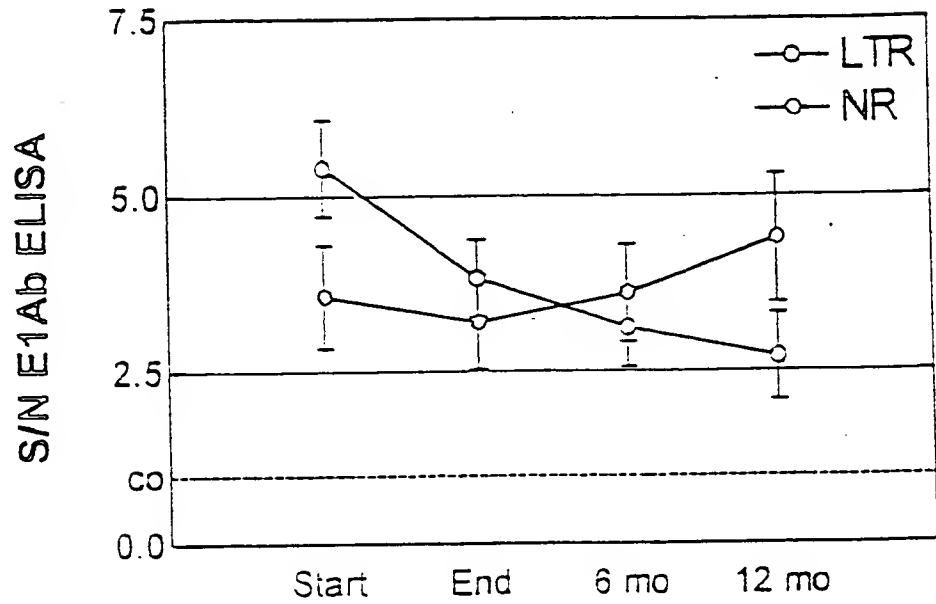


Fig. 36B

E2 Ab

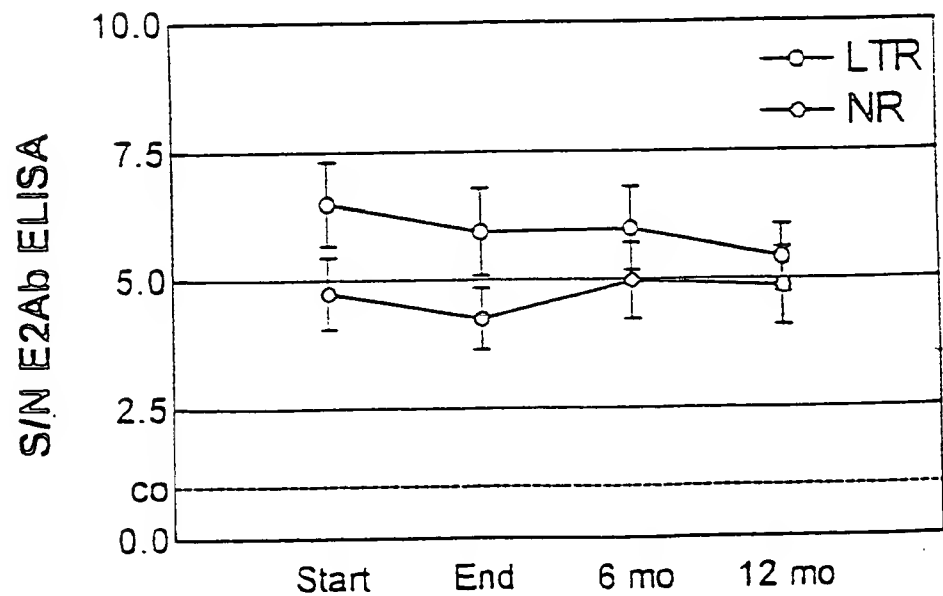


Fig. 37A
Non Responders

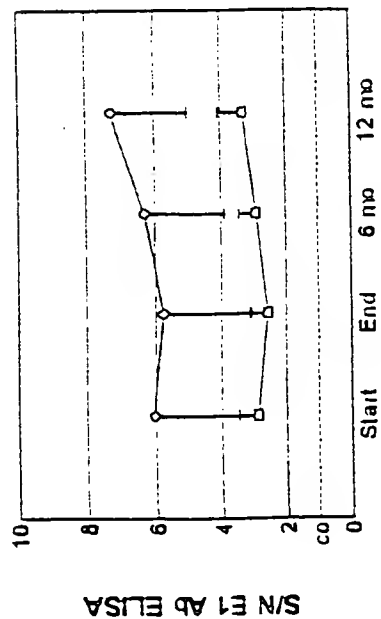


Fig. 37B
Long Term Responders

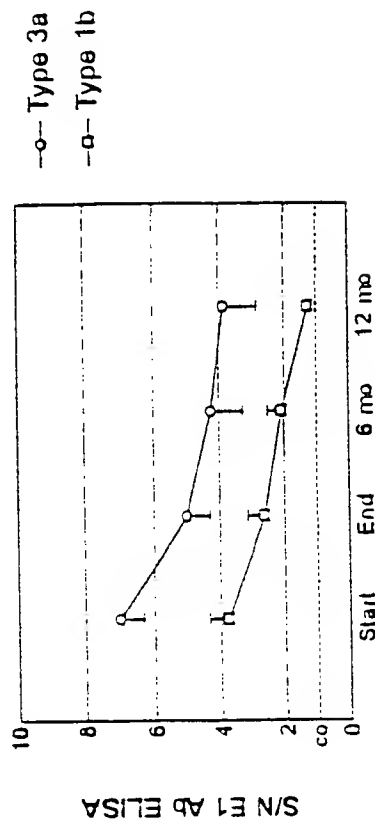


Fig. 37C
Type 1b

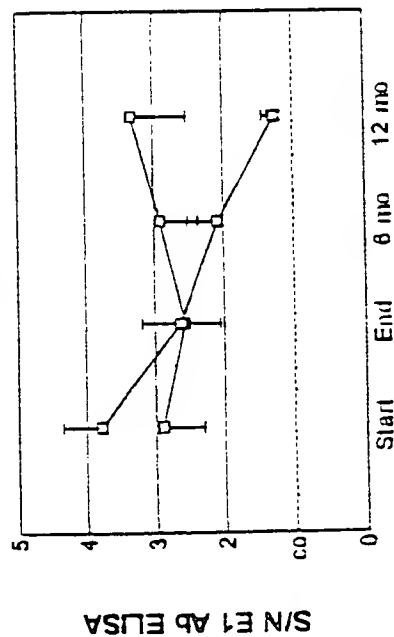


Fig. 37D
Type 3a

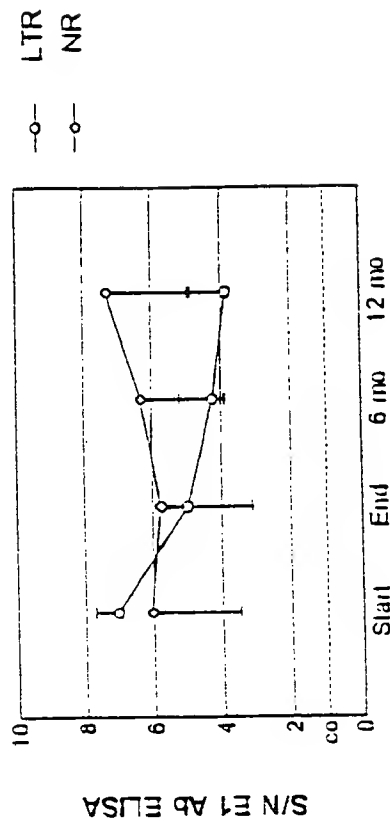
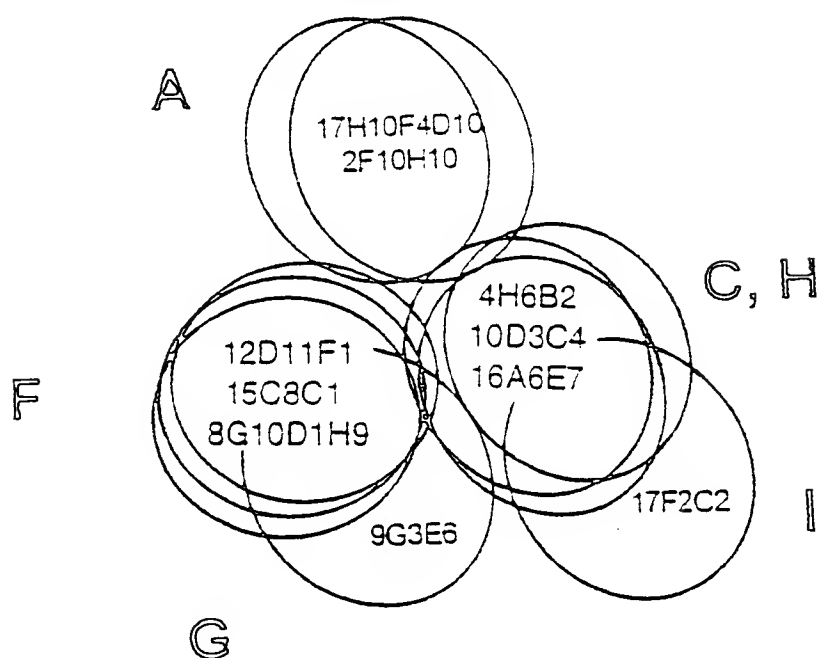


Fig. 38

Relative Map Positions of
anti-E2 monoclonal antibodies



105211-09055560

Fig.39

PARTIAL DEGLYCOSYLATION
OF HCV E1 ENVELOPE PROTEIN

Endoglycosidase H (Endo H)		Glycopeptidase F (PNGase F)	
0µl	0.6µl	0µl	400µl
0.6µl	6µl	0.04µl	40µl
6µl	60µl	0.4µl	4µl
60µl	0.6µl		
0.6µl			
6µl			
60µl			
0.6µl			
6µl			
60µl			



PARTIAL TREATMENT OF HCV E2\E2s ENVELOPE PROTEINS BY PNGase F

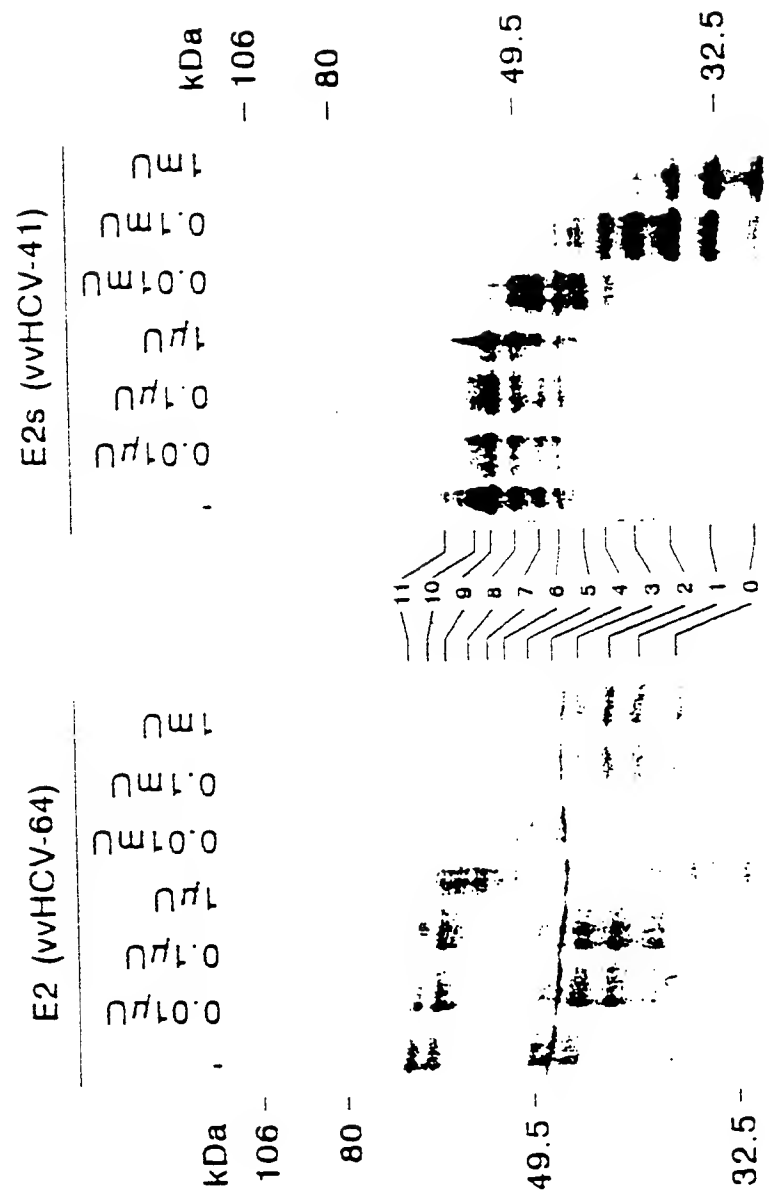


Fig. 40

Fig. 41 *In Vitro* Mutagenesis of HCV E1 glycoprotein

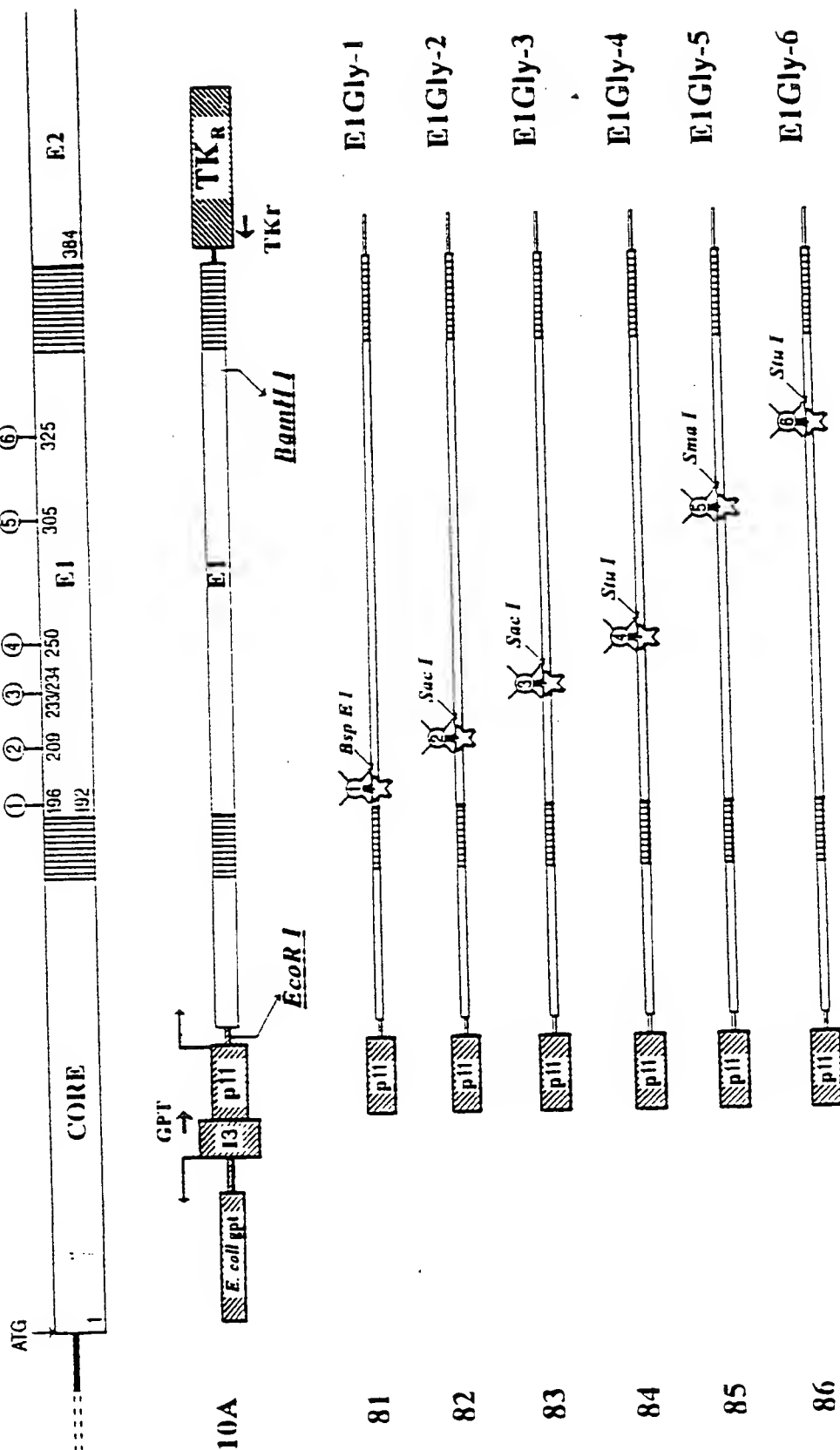
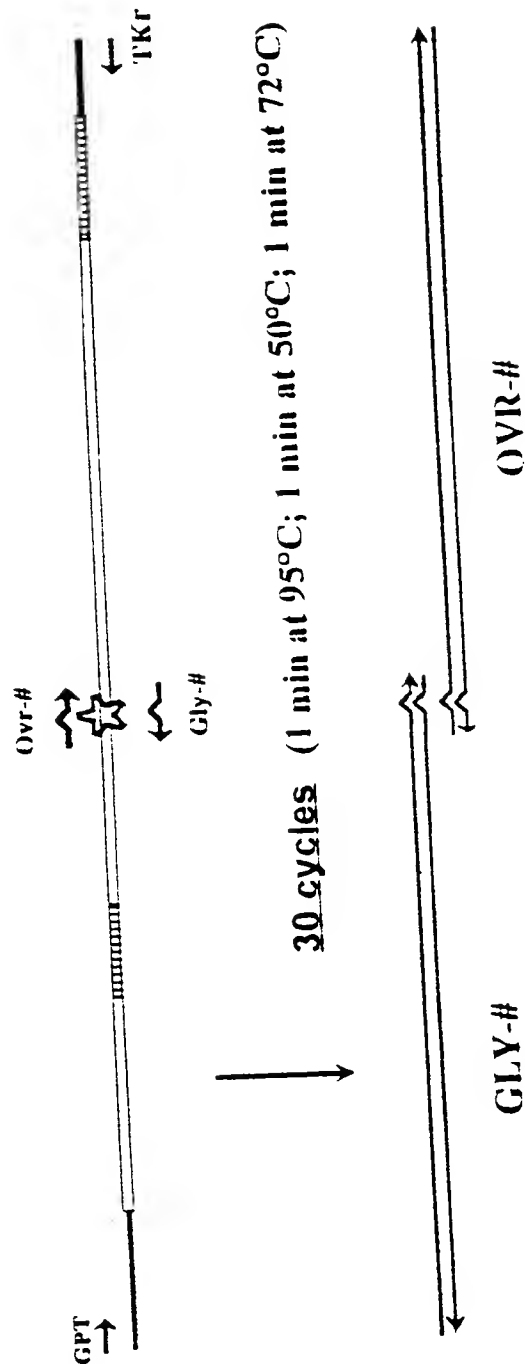


Fig. 42A *In Vitro* Mutagenesis of IICV E1 glycoprotein



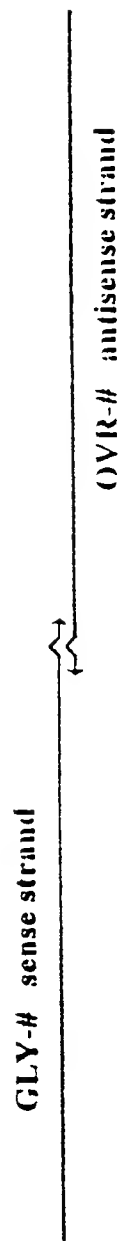
1. First step of PCR amplification (Gly-# and Ovr-# primers)



2. Overlap extension and nested PCR

Fig. 42B

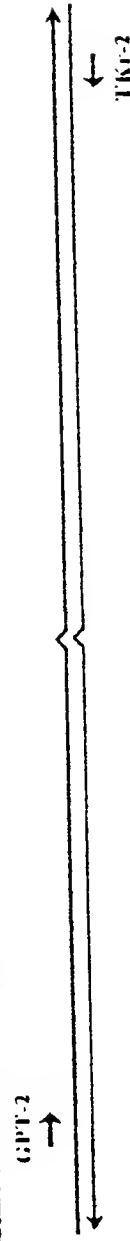
a. Overlap extension



↓
2 cycles (1 min at 95°C; 1 min at 50°C; 1 min at 72°C)



b. Nested PCR amplification (GPT-2 and TKr-2 primers)



↓
25 cycles (1 min at 95°C; 1 min at 55°C; 1 min at 72°C)

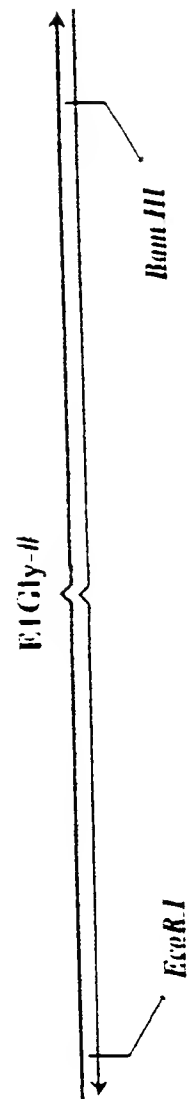
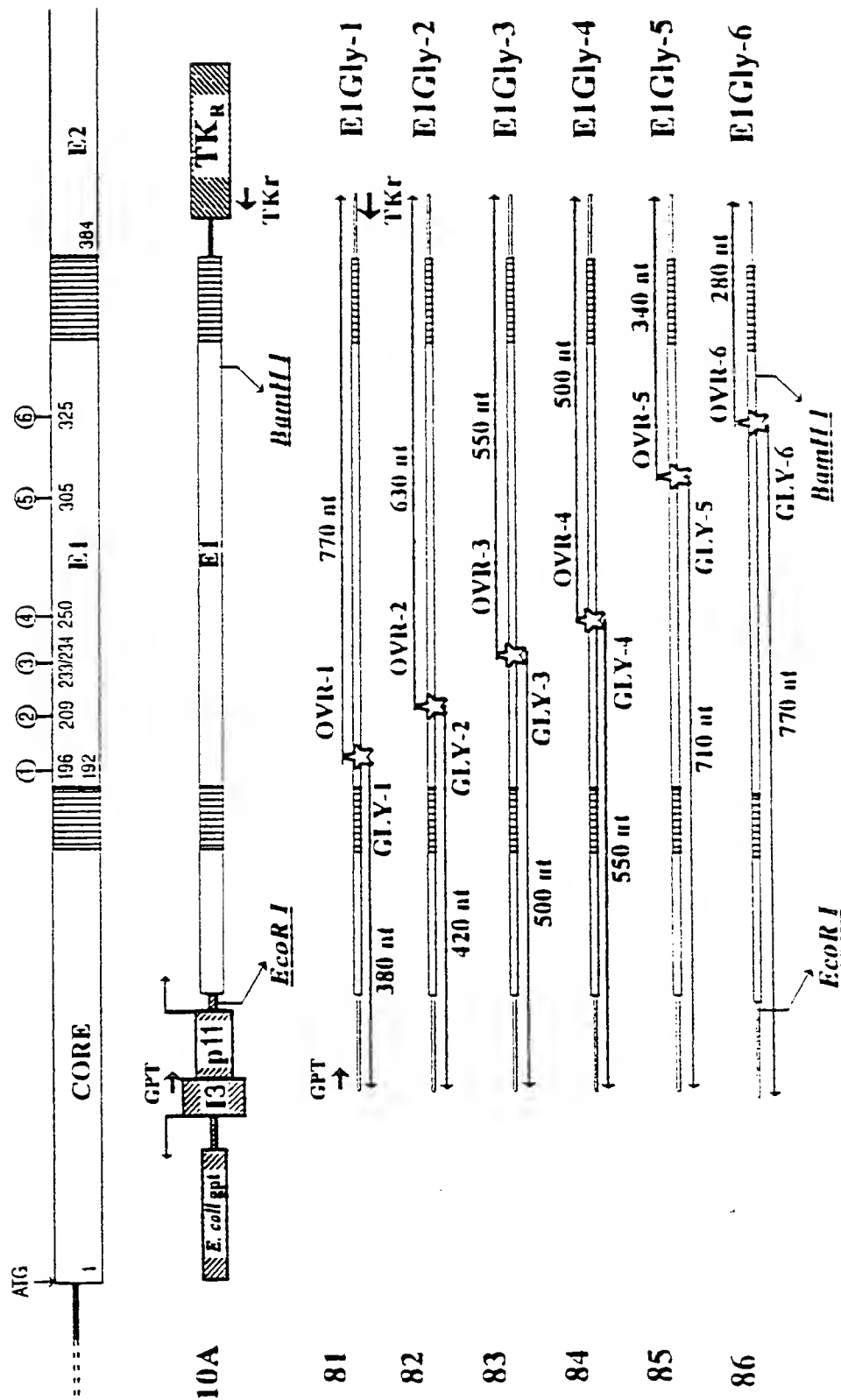


Fig. 43 *In Vitro* Mutagenesis of HCV E1 glycoprotein



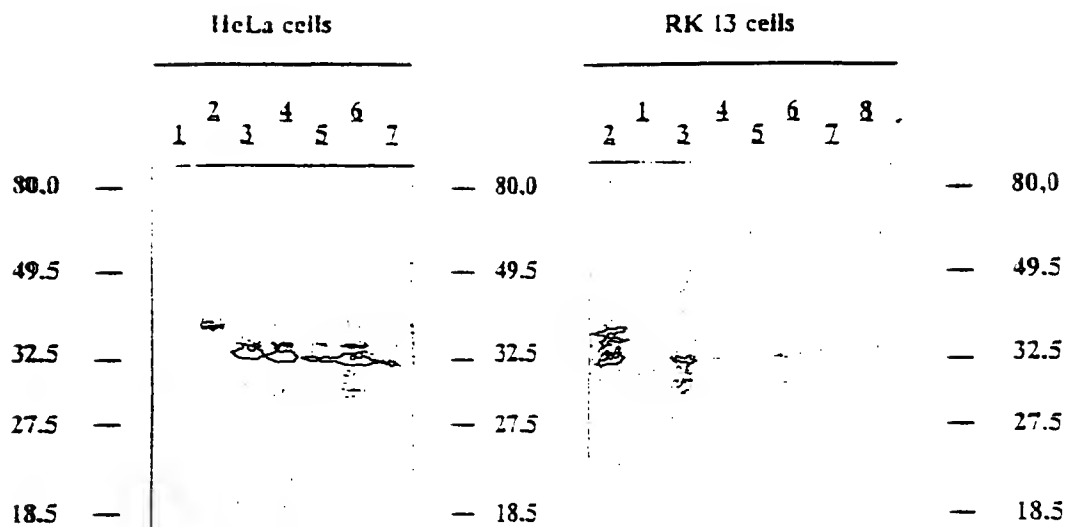


Fig. 44A

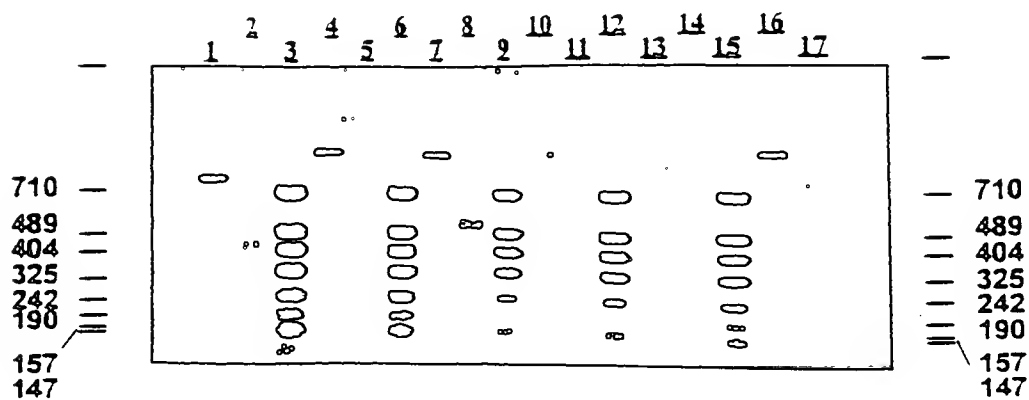


Fig. 44B

[REDACTED]

KDa 119 67 43 29 18

! ! ! ! !


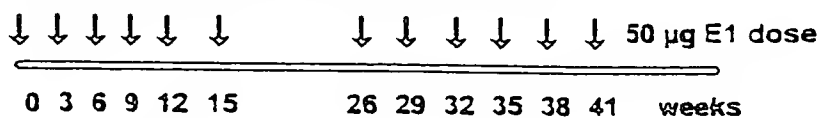


Fig. 47

	age (years)	HCV infection (years)	genotype
Marcel	17	9	1a
Peggy	21	16.5	1b
Fenna	15	9	1a
Yoran	12	none	
Marti	12	none	

chronic carriers (strong T-cell adjuvant)



naive (alum)



Fig. 48

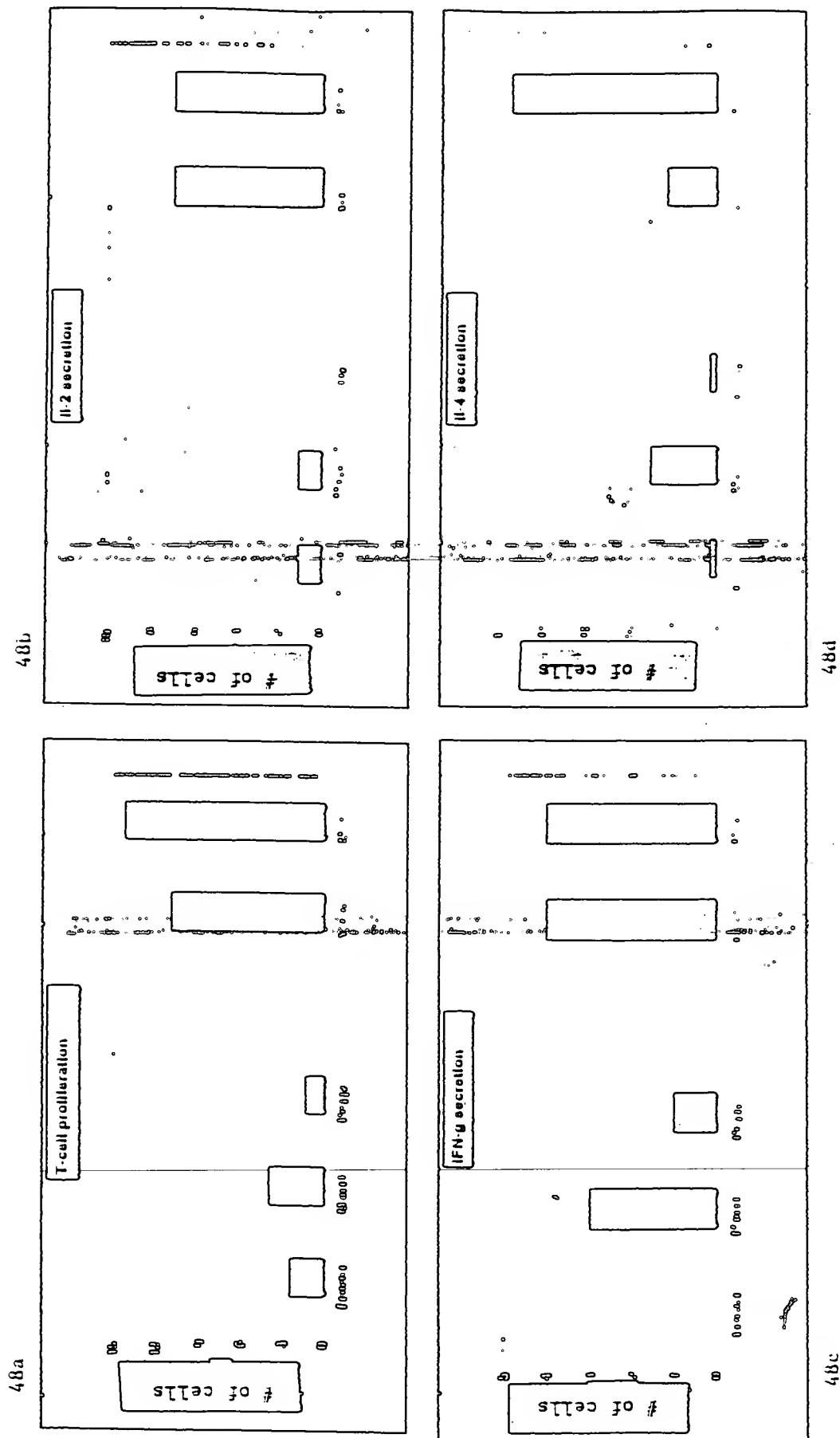
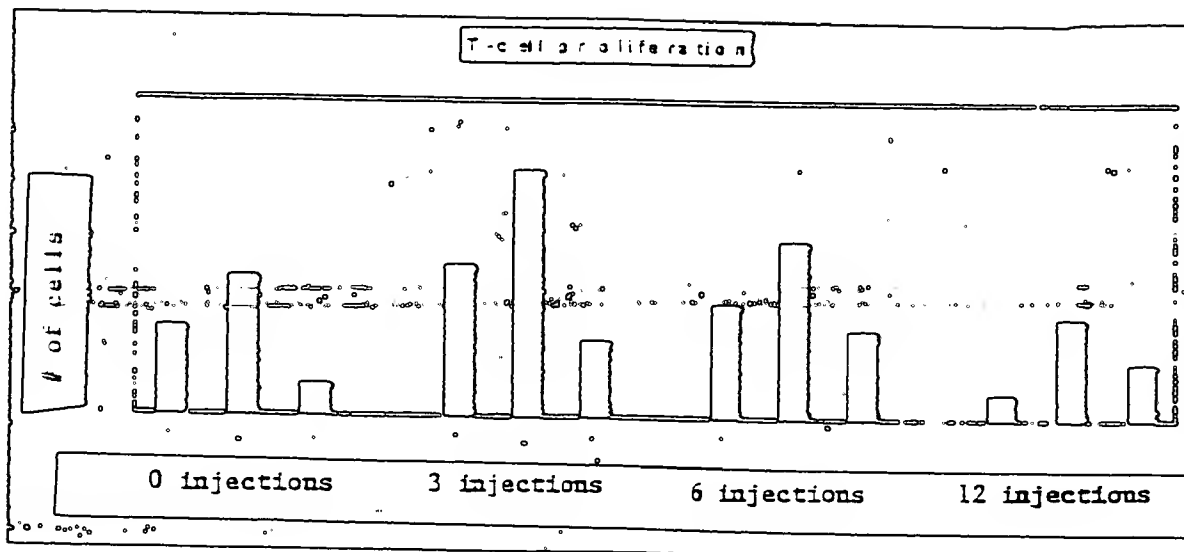


Fig. 49



1 Fem m a, 2 Mar cel, 3 Peggy

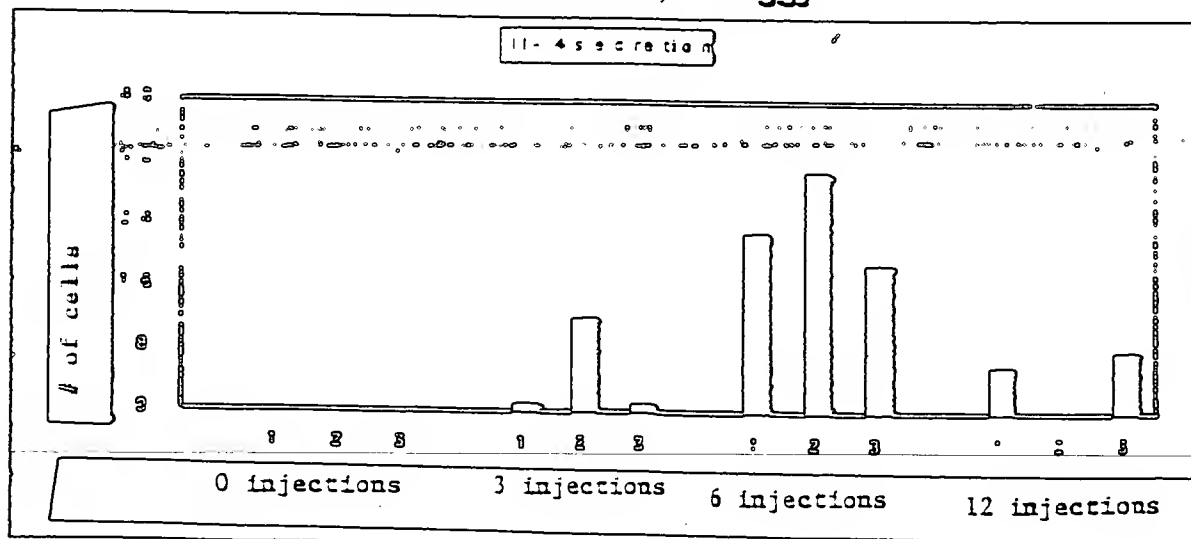
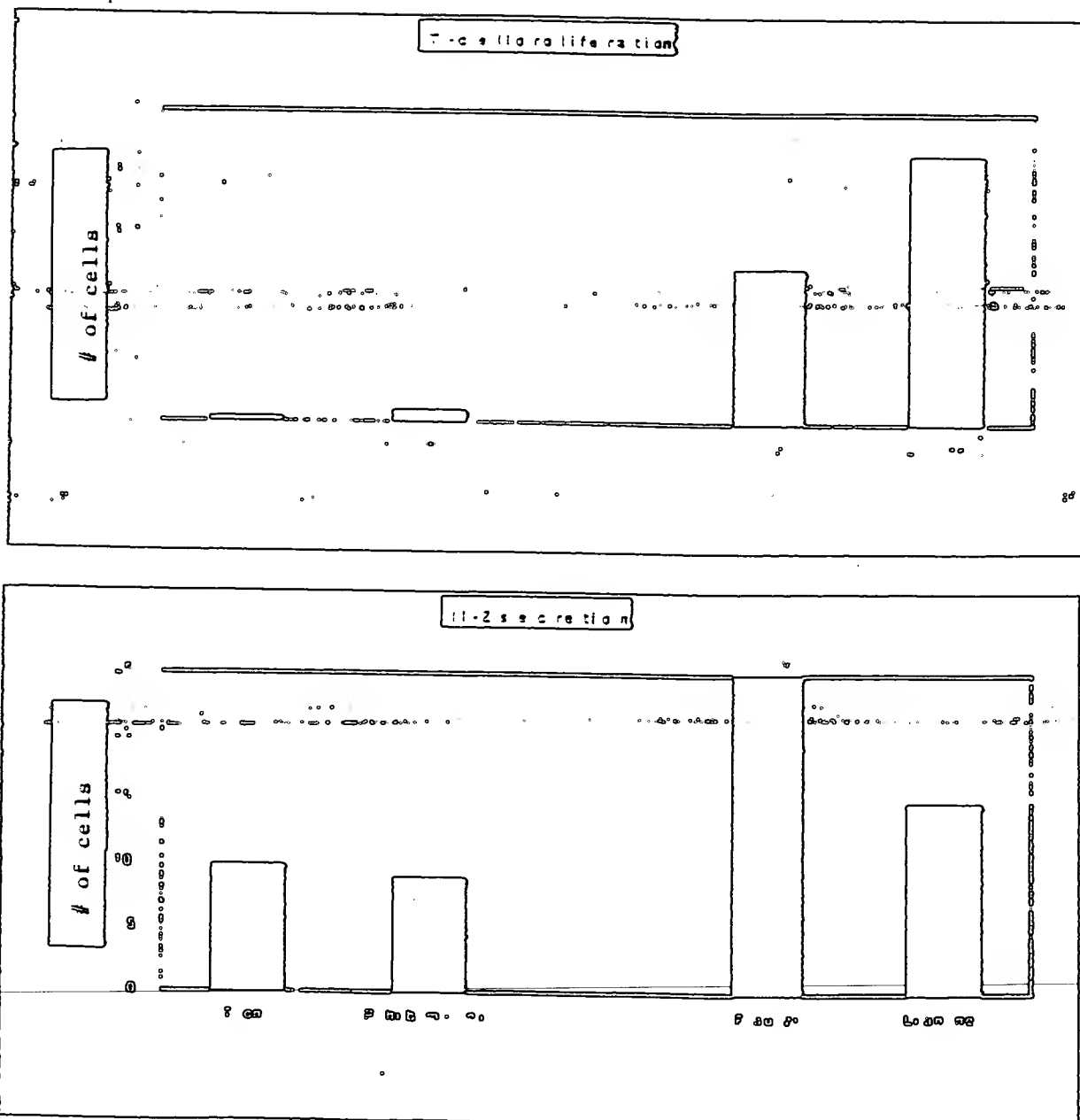


Fig. 50

Fig. 50



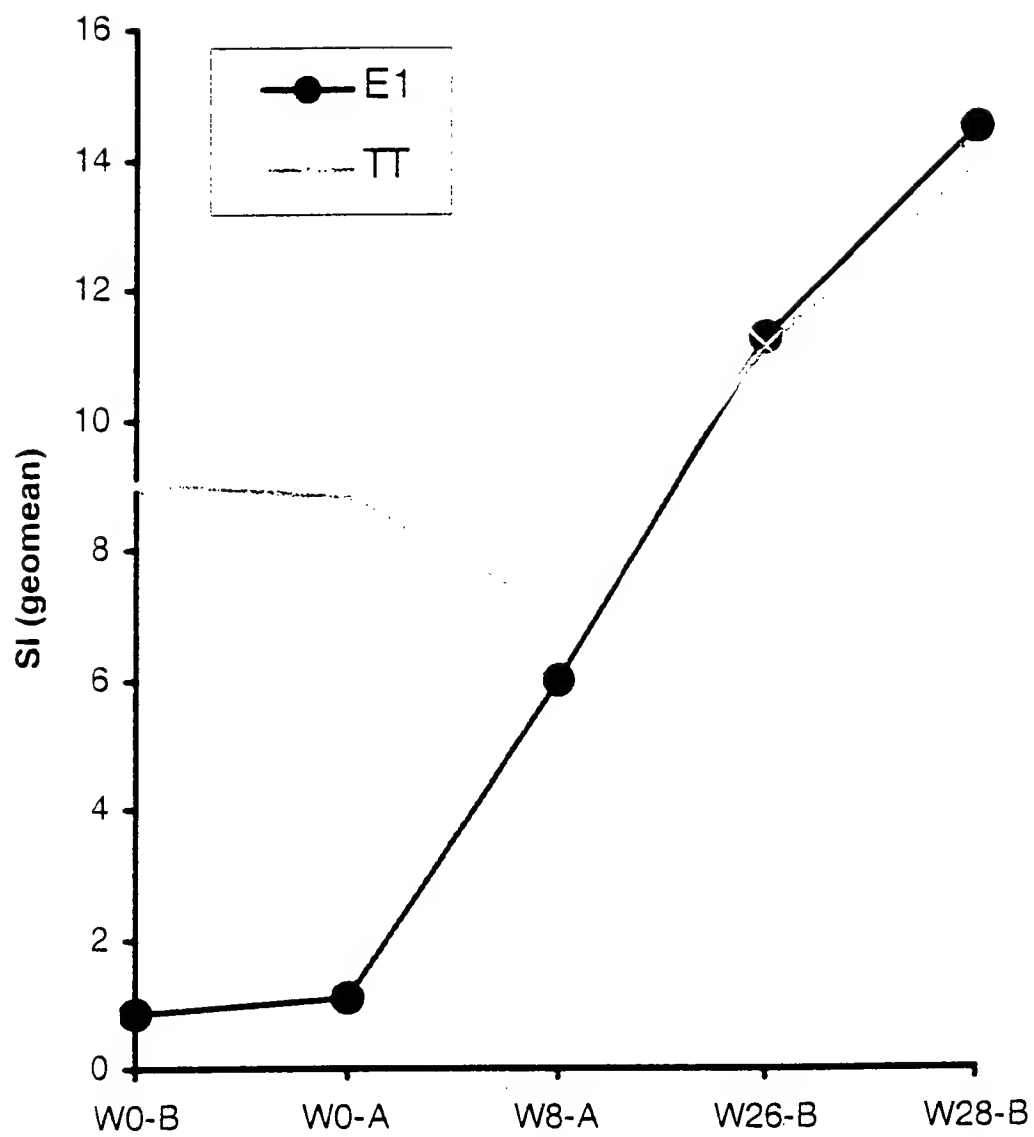


Fig 51

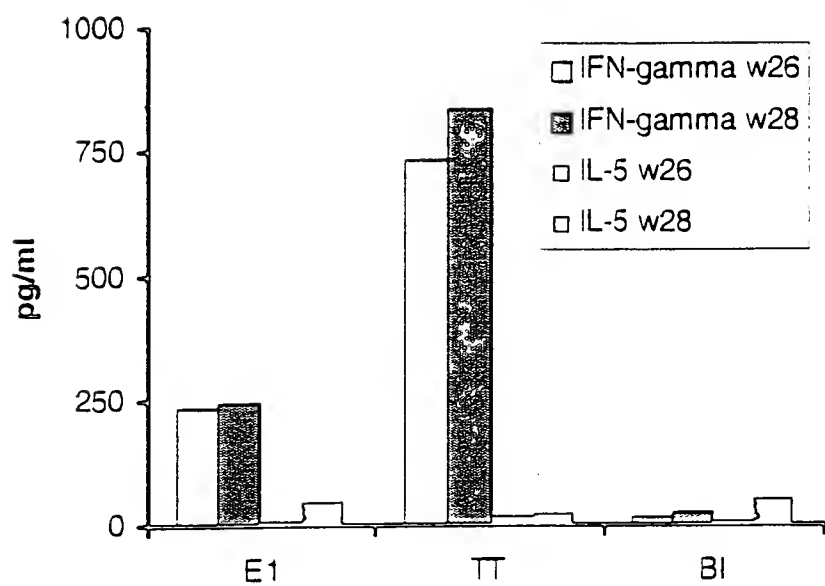


Fig 52

[illegible]

A scatter plot showing the relationship between S1 (Y-axis, 0 to 30) and Year (X-axis, 19626 to 19636). The data points are categorized by year, with 1962-1963 being the primary focus. The plot shows a general trend of increasing S1 values over time, with a significant peak around 19631.

Figure 10: Scatter plot of $|S|$ versus index for the 1626-1636 range. The y-axis is labeled $|S|$ and ranges from 0 to 30. The x-axis shows indices from 1626 to 1636. Data points are mostly near zero, with a notable outlier at index 1632 reaching approximately 7.